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PRINCIPLES OF SURGERY.

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PREFACE.

A MODERN work on the principles of surgery in the English language has become a generally and well-recognized necessity. The recent great discoveries relating to the etiology and pathology of surgical diseases have made the text-books of only a few years ago old and almost worthless. The many treatises on surgery, by American and English authors, which have made their appearance in rapid succession during the last ten years or more, are replete with valuable practical information, but most of them are defective in those parts relating to the matter treating of the fundamental principles of the art and science of surgery.

It has been my aim to write a book for the student and general practitioner which should, at least in part, fill this gap in surgical literature, and which should serve the purpose of a systematic treatise on the causation, pathology, diagnosis, prognosis, and treatment of the injuries and affections which the surgeon is most frequently called upon to treat. The successful study and practice of any branch of the healing art require a thorough knowledge of the principles upon which it is based. The student who has mastered the principles of surgery will have no difficulty in applying his knowledge in practice, while the one who has burdened his memory with numerous details to meet special indications is always at a loss in making prompt and judicious use of his therapeutic resources when confronted by rare lesions or unexpected emergencies.

In writing this book it has been my intention to keep in constant view the difference between the cellular processes, as we observe them in regeneration and inflammation, and to connect the modern science of bacteriology more intimately with the etiology and pathology of surgical affections than has heretofore been done by most authors who have written on the same subjects. In showing the direct etiological relationship which exists between certain pathogenic micro-organisms and definite pathological processes, I have frequently made liberal use of the experimental and clinical material contained in my work on "Surgical Bacteriology." When the subject of tumors was reached it was found that the manuscript had become so voluminous that it was deemed advisable to publish the volume without this part of the intended scope of the work,—an arrangement to which the publisher kindly gave his consent. It is the author's intention to make good this defect by the preparation, in the near future, of a special work on "The Pathology and Surgical Treatment of Tumors."

With few exceptions the sources from which my information was taken are not given, as a copious bibliography would have required considerable valuable space. At the same time the author hopes that he has presented the views and opinions of the authorities quoted with sufficient clearness and thoroughness to render a resort to the original articles, in most instances, unnecessary. Among the text-books which I have consulted I desire to mention the following: Histology: Klein, Schäfer, Heitzmann, and Satterthwaite. Pathology: Klebs, Hamilton, Birch-Hirschfeld, Paget, Virchow, Coates, Lebert, Rindfleisch, Delafield, and Prudden. The Principles of Surgery: König, Hueter-Lossen, Landerer, Billroth-Winiwarter, and Van Buren. Bacteriology: Fluegge, Baumgarten, and Cruikshank. The illustrations were selected from modern text-books not readily accessible to the average student.

A prolonged absence from home made it impossible for the author to attend to the proof-reading, and he asks the indulgence of the reader for any imperfections which may appear in the book from any sources for which he cannot be held personally responsible.

Should this volume become the means of lightening and facilitating the student's work in acquiring a thorough knowledge of the fundamental principles of surgery, and of serving as a useful source of information for the busy general practitioner, the author will feel abundantly rewarded for the many sleepless nights which were required in its preparation.

N. SENN.

MILWAUKEE, October, 1890.

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PRINCIPLES OF SURGERY.

CHAPTER I.

REGENERATION.

REGENERATION includes a multitude of processes which are intended to repair the normal physiological waste of the tissues in the living body or to restore tissues lost by injury or disease. In the human body normal regeneration or repair of tissues is a physiological process, which is essential for the maintenance of the anatomical perfection and functional activity of the different tissues and organs. In a condition of perfect health, in the full-grown body, the normal waste incident to the increasing activity of the tissues is balanced by this reparative process, while during the development of the body an excess of material is added upon which depends the increase of tissue which constitutes growth. If cell-destruction is in excess of cell-reproduction atrophy is the inevitable result, and if the function of regeneration is completely suspended death must necessarily ensue, the blood being the first tissue the seat of extreme atrophic changes, soon to be followed by similar changes in all the tissues, resulting in diminution of function proportionate to the degree of atrophy, and, finally, death from marasmus.

Studied from a surgical aspect, regeneration includes the process observed in the healing of wounds produced by a trauma and the complete or partial restoration of parts damaged or destroyed by the action of chemical substances, extremes of cold or heat, and the various destructive inflammatory processes caused by the presence of specific pathogenic micro-organisms. Regeneration and inflammation are distinct conditions, which should no longer be confounded or considered from the same etiological and pathological stand-point. An ideal regeneration takes place without inflammation provided the seat of injury or tissue-destruction remains aseptic; that is, free from pathogenic microbes. On the other hand, a regenerative process within or around an inflammatory focus can only be established in tissues in which the cause which has produced the inflammation has not been sufficiently intense to destroy the protoplasm of the cells. Under these circumstances the reparative process is initiated at a time when the cause which has given rise to the inflammation has ceased to be active, or in tissues not deprived of their vegetative power by its action. In a circumscribed suppurative inflammation the cells exposed to the direct action of the pus-microbes and their ptomaines are destroyed, and the process of repair starts from the abscess-walls and their immediate vicinity, from tissues which have retained their power of cell-proliferation. Any organ the seat of a tubercular infection, in which the parasitic cause is not sufficiently intense to destroy the vitality of the cells, retains its normal structure and function by virtue of this intrinsic power of regeneration of its cells. All reparative processes consist of homologous cell-development, and the new tissue resembles, anatomically and physiologically, the fixed cells from which it is produced. The legitimate succession of cells is now a well-established law in pathology as well as embryology, and, according to this tissue, is never produced by substitution of function. According to this histogenetic law, each cell-element possesses an intrinsic vegetative power from the earliest embryonal development throughout life, which, in case of loss of tissue by injury or disease, enables it to produce its own kind and never any other materially different histological structure. In conformity with this general law of tissue-production, an injury or defect of a nerve-fibre is repaired by proliferation from pre-existing cells which compose this structure, epithelial cells are produced only by epithelial cells, new vessels are formed from cells which exist in a normal vessel-wall, etc. From this stand-point will be considered—

I. HEALING OF WOUNDS.

A wound may be defined as a sudden solution of continuity of any of the tissues of the body caused by the application of mechanical force. A wound is open or subcutaneous according as the surface covering the skin or mucous membrane has been cut or torn or has remained intact. Since the introduction of the antiseptic treatment of wounds, the classification into open and subcutaneous wounds is no longer of the same practical importance, as an open wound, under careful antiseptic treatment, is at once placed under the same favorable conditions for a satisfactory and rapid healing as a subcutaneous wound. All wounds, irrespective of the anatomical structure of the tissues involved, heal by the production of new material from pre-existing fixed tissue-cells. The fixed tissue-cells at the site of injury being endowed from earliest embryonal life with a peculiar power of adaptation to existing conditions surrounding them, assume active tissue proliferation, and the embryonal cells thus produced constitute the granulation-tissue, which, toward the completion of the healing process, is transformed into mature cells, representing the tissue or tissues which have undergone the reparative process.

IMMEDIATE OR DIRECT UNION.

Since the time of John Hunter a great deal has been said and written on immediate or direct union of wounds. Hunter believed that this method of healing would be accomplished within a few hours, and without the interposition of new material between the accurately coapted surfaces. Macartney was a supporter of this view, as will be seen from the following: "The circumstances under which immediate union is effected are the cases of incised wounds that admit of being, with safety and propriety, closely and immediately bound up. The blood, if any be shed on the surface of the wound, is thus pressed out, and the divided blood-vessels and nerves are brought into perfect contact, and union may take place in a few hours; and, as no intermediate substance exists in a wound so healed, no mark or cicatrix is left behind." Paget applies this method of healing to large wounds where rapid union is accomplished, and where, on examination, no interposed tissue is found between their edges. Such a case came under his own observation. A patient on whom he had performed an operation for the removal of a carcinomatous breast died from an attack of erysipelas a few days later. Examination showed that firm union had taken place apparently without any intermediate material. He also made three experiments on rabbits for the purpose of studying this rapid method of repair. The hair was removed, the skin incised, and the wound accurately sutured. Three days later he examined the parts, and found the wound quite firmly united, without any macroscopical evidences of inflammation. On microscopical examination, he found some exudation material in the immediate vicinity of the wound.

Among the more modern investigators, we find Thiersch still upholding the possibility of immediate union by direct cohesion of similar parts. He studied the repair of wounds in the tongue of guinea-pigs. The tongue was incised in a longitudinal direction, and the parts were examined a few hours to several days after the injury had been inflicted. Before sections were made for microscopical examination the lingual vessels were injected with liquid glue stained with carmine. In specimens where the wound was only a few hours old he found, at least, parts of the wound firmly adherent, and on microscopical examination he satisfied himself that the connective tissue, saturated with blood and plasma, had formed an immediate and permanent union. He described also a plasmatic circulation in the wound which he considered of great importance for the nutrition of the tissues. He believed that these new channels, by becoming paved with the adjacent connective cells, could be transformed into permanent blood-vessels.

The same section examined under a higher power furnishes a good estimation of the part taken by the fixed tissue-cell in the repair of the wound.

Some surgeons still believe in immediate union in the repair of wounds of nerves, as many cases have been reported where complete restoration of function was claimed to have been established within a few hours after nerve suture. Such observations are not free from criticism, because functional results after nerve suture may lead to wrong conclusions, as restoration of function in distal parts may be owing to the presence of other nerves which reach such parts, and partly it may be due to physical conduction of irritation. The occurrence of immediate union was doubted by O'Halleran, a distinguished contemporary of Bell, as may be learned from the following quotation: "I would ask the most ignorant tyro in our profession whether he ever saw, or heard even, of a wound, though no more than one inch long,

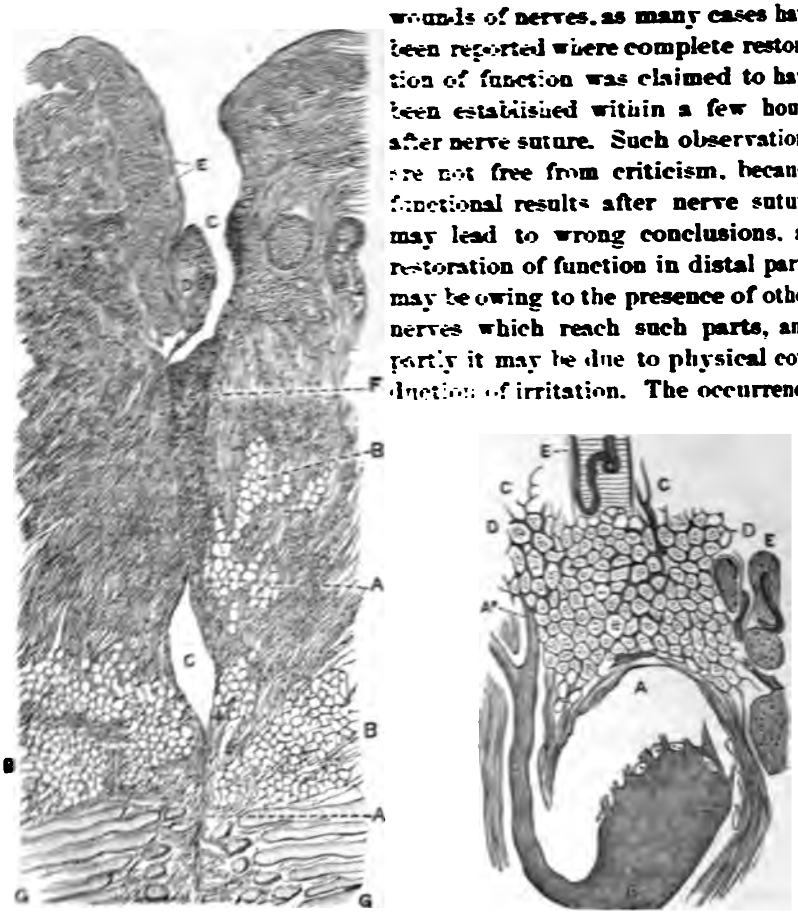

FIG. 1.—A WOUND TWENTY-SIX HOURS OLD. (*Thiersch.*)

A. Coaptated parts apparently united. Tissues only slightly stained with coloring material of blood; few [illegible]. B, B. Spaces between wound-surfaces filled with red and white blood-corpuscles, some of the former well preserved, others showing various degrees of disintegration; between them, œdematous connective-tissue fibres. C, C show that these fibres are continuous with the connective tissue of the wound-surfaces. Surface of wound coaptation imperfect; the epithelial cells dip down into the wound. D. A separated cone of new tissue. B. Infiltration of fatty tissue with blood and leucocytes. G, G. Divided muscular fibres, with escaped pieces which have partly undergone colloid degeneration. (Hartnack, Obj. 4, Oc. 2.)

united in so short a time," adding, "These tales are told with more confidence than veracity; healing by inosculation, by the first intention, by immediate coalescence without suppuration is merely chimerical and opposite to the rules of nature."

Gussenbauer repeated the experiments of Thiersch and Wywodzoff on the healing of wounds in the tongue of guinea-pigs, and came to entirely different conclusions. In wounds eight to twelve hours old he found that the margins formed an elliptical space, the separation being widest in the middle. The divided muscular fibres had retracted, imparting to the wound an uneven surface, which was covered with a layer of reddish, gelatinous material. In recent wounds the space is filled with blood-corpuscles which are often much changed in color, size, and shape. In wounds twenty-four to forty-eight hours old the material between the surfaces of the wound presented a reticulated appearance, each one of the spaces corresponding to a blood-vessel. Contrary to Thiersch, he asserts that in this substance no connective tissue can be found; the reticulated structure he attributed to the presence of fibrin, the coagulum infiltrating at the same time the adjacent tissues. He believes that the

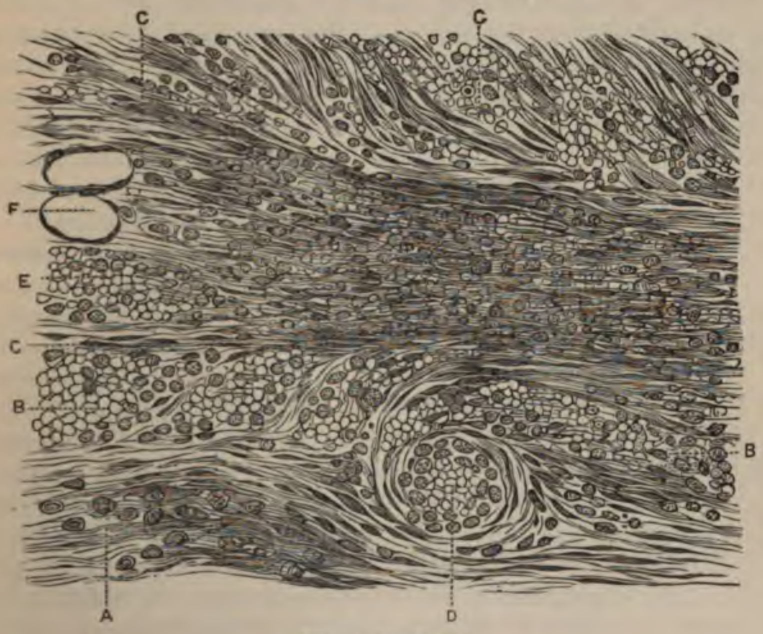

FIG. 2. (*Thiersch.*)

A, embryonal cells showing karyokinetic figures; B, lymph-spaces; C, striped masses infiltrated with red blood-corpuscles in various stages of disintegration; D, blood-vessel; F, fat-tissue. (Hartnack, Obj. 8, Oc. 4.)

parenchyma fluid takes part in the formation of the coagulum. He was unable to verify, by his own observations, the existence of the plasma channels described by Thiersch. When the wound-surfaces were kept accurately approximated he found few blood-corpuscles, but the net-work of fibrin was never found absent. In hare-lip operations and incised wounds of the face and scalp, if uninterrupted apposition is maintained for a day or two, the parts are found so firmly glued together that the belief that immediate union had taken place might still be maintained from a superficial examination, but a microscopical examination will always reveal the conditions described by Gussenbauer, and the union is therefore only apparent, and not real. The surfaces of the wound have become adherent by the interposition of an adhesive material. A certain amount of coagulation necrosis takes place in every wound, and the material thus formed serves as a cement-substance which temporarily glues the parts together. This mechanical union, the result of destructive chemical changes in the extravasated blood, is the form of union which has been wrongly interpreted and described as immediate union. This primary adhesion occurs most readily in wounds of dense vascular tissue and where approximation and fixation of the edges of the wound are most thoroughly secured,—conditions which favor the subsequent definitive healing of the wound by the interposition of new tissue.

UNION BY PRIMARY INTENTION.

Organic union, the union aimed at in the treatment of all wounds, is only obtained by tissue-proliferation from the fixed cells of the injured parts, and is completed only after restoration of the continuity of the divided structures, and the return, partial or complete, of the functions suspended by the injury or disease. Return of structure and function to an at least approximately normal standard implies a return of the interrupted circulation by the formation of new blood-vessels; in other words, organic union cannot be said to have taken place without an adequate supply of new blood-vessels in the new tissue which form a capillary net-work between the divided blood-vessels. Such a union, even under the most favorable circumstances, cannot be established in less than six to eight days, and its attainment may require weeks and months. The next method of repair described by John Hunter was union by adhesive inflammation. Absence of suppuration and rapid union have always been considered as essential features of this mode of healing, and corresponds to the healing of wounds *per primam intentionem*, an expression which, for obvious reasons, has been retained in modern literature to distinguish it from the method of healing *per secundem intentionem*, where the reparative process is often indefinitely delayed by suppuration. All wounds which heal without suppuration heal by primary union, either *without* or *with* visible granulation tissue. An ideal result is obtained if the divided surface unites throughout and the repair in the depth of the wound is accomplished during the same time underneath the united skin or mucous membrane. If there has been a considerable loss of surface tissue and the superficial portion of the wound cannot be approximated, or, if rapid healing at the surface of the wound fails to take place, the wound heals slowly by the formation of a larger amount of granulation tissue, and yet, if suppuration does not complicate the process it must be said that the wound has healed by primary union. This method of healing was exceedingly rare before antiseptic surgery was practiced, but since that time it is of frequent occurrence. *All wounds which heal without suppuration heal without inflammation. All inflamed wounds suppurate; the reparative process is delayed until the inflammation has subsided.* The proper modern classification of wounds in reference to the method of repair consists in a distinction between (1) aseptic wounds and (2) infected wounds. *Aseptic wounds—that is, wounds not contaminated with pathogenic micro-organisms—heal without inflammation.* An aseptic wound, as a rule, is painless, and does not present any of the other witnesses of inflammation. The slight swelling and, perhaps, redness are the result of mechanical disturbances of the circulation, and subside with the formation of an adequate collateral circulation; hence, from an etiological and pathological point of view, we have no legitimate right to apply the term inflammation to such a method of repair. Koenig makes the statement that the product of tissue-proliferation in the healing of an aseptic wound is not in excess of the local demand; hence, the process is purely one of regeneration, and not inflammation. Hueter was one of the first who insisted on limiting the meaning of the term *inflammation*, which he wished to have applied only to destructive processes caused by the action of specific microbes. In an aseptic wound the fixed tissue-cells assume tissue-proliferation, by virtue of their intrinsic vegetative power, within a few hours after the injury has been inflicted, and all the permanent material utilized in the process of repair is derived from this source. The leucocytes serve a useful purpose in the temporary closure of divided capillary vessels and in the formation of the temporary cement-substance by which the surfaces of the wound are mechanically glued together, and, lastly, as food for the embryonal cells, *but they take no active part in the production of new tissue.*

In studying the process of healing in wounds as well as in the consideration of regeneration in general, it is of the greatest importance to become familiar with the histological changes which precede and attend the formation of new tissue; hence, in this connection should be given a description of

KARYOKINESIS.

Karyokinesis, or karyomitosis, as described by Flemming, is the indirect reproduction of cells as compared with direct cell-division by segmentation. It is a process by which the net-work of chromatin threads within the nucleus undergoes great development, and is subject to certain transformations of form, which are instrumental in effecting division of nucleus and cell. The term *karyokinesis* was first used by Schleicher, and the first accurate description of the process, as seen in the cells of a number of animals, simple in form and structure, was given by Bütschli in 1876. The modern definition of a cell is much more complicated than that given by Schleiden and Schwann, as recent researches have shown that it is not such a simple structure as it was formerly believed to be. When we speak of a cell now we mean a mass of circumscribed living substance, with or without an envelope, which contains as an essential element in its interior a nucleus, with the property of forming new compounds out of substances taken into it, and is capable of reproduction by division. Both the nucleus and cell are composed of threads and intermediate substance. The cell-body consists of threads somewhat irregularly distributed, seldom forming a net-work, embedded in a homogeneous substance. The nuclear threads stain with hæmatoxylon and safranin, and hence are called chromatin threads, which are arranged in a net-like figure, the meshes of which are filled with a substance which cannot be stained, and hence is named by Flemming *achromatine*. The nucleus is surrounded by a membrane composed of two layers; the inner can be stained, but not the outer. The nucleoli, usually multiple, are made up of a substance more refractile than the structures described in the nucleus. They are round and smooth, and

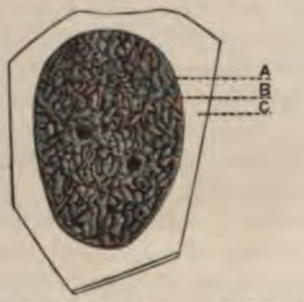

FIG. 3.—QUIESCENT NUCLEUS. EPITHELIAL CELL OF SALAMANDER ENTERING UPON THE "GLOMERULAR" PHASE. (*Flemming.*)

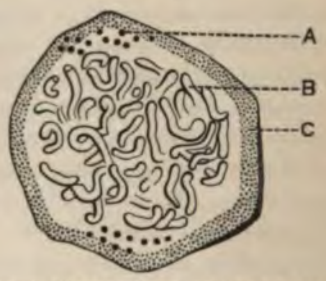

FIG. 4.—LIVING CELL OF SALAMANDER. (*Flemming.*)

A, granules aggregated round a pole of the cell; B, coils of "glomerular" net-work; C, cell-body.

either suspended in the net-work or between the threads. The nucleus in a cell that is not in a condition of functional activity is said to be in a quiescent or resting state.

At this time the chromatin threads become transformed into a sort of skein, formed apparently of one long, convoluted thread; the inner layer of the nuclear membrane and nucleoli disappear, or are incorporated into the achromatine substance of the nucleus. The development of the net-work of the chromatin substance in the nucleus undergoes five phases until complete division of the nucleus and cell has been effected.

Phase I. The first change indicative of beginning karyokinesis, according to Flemming, is the formation within the cell-protoplasm of two poles opposite to each other and near the nucleus.

The next change noticed is that in the nucleus: the chromatin threads become plainer, thicker, and more convoluted. This increase of chromatin substance is the result of longitudinal splitting of its threads. The achromatine layer of the nuclear envelope increases in thickness, while the inner layer has become a part of the chromatin net-work.

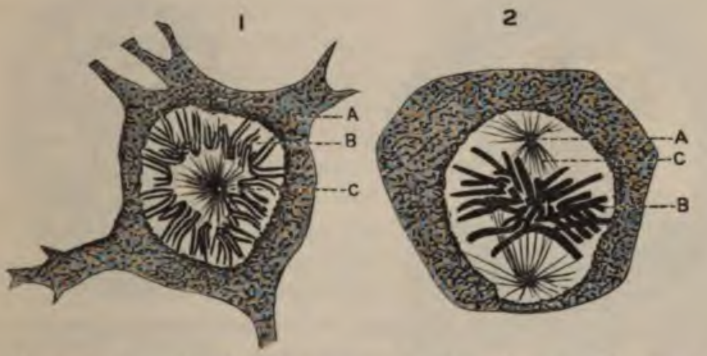

FIG. 5.—ENDOTHELIAL CELLS; ABDOMEN OF SALAMANDER. (*Flemming.*)

1. Surface view of nuclear net-work; A, cell-body; B, threads of net-work; C, one of the poles with the achromatine threads radiating from it. 2. Equatorial view of a corresponding cell; A, one of the poles; B, the nuclear net-work seen on edge; C, the achromatine threads forming a spindle between the poles.

Phase II. During this stage the chromatin threads are drawn out into loops with long limbs. This arrangement imparts to the looped net-work the figure of an aster, or star.

In the middle of the star is a clear space, which does not stain and is occupied by achromatine substance. In animal cells the greater portion of the space within the nuclear membrane is filled with chromatin threads, while in vegetable cells the achromatine substance predominates. The nuclear spindle in the centre of the achromatine substance (Fig. 4, C), according to Strassburger and Bütschli, consists of fine, colorless fibres, which do not stain at all, or only slightly, by using special nucleus-staining reagents, and on this account the achromatine threads probably contain no nuclein.

Phase III. The star-shaped mass of nuclear threads divides into two equal portions, with the angles of the loops to the poles, and their limbs partly obliquely, partly perpendicularly to the equator of the nucleus.

The equatorial disk is formed in this manner, and indicates the completion of this phase.

Phase IV. This phase begins with a separation of the threads at the equator, and ends with concentration of the threads in each polar segment of the cell.

As the number of loops in each segment is the same as in the old nucleus, it may be conjectured that the halves of each thread separate into the two daughter-stars.

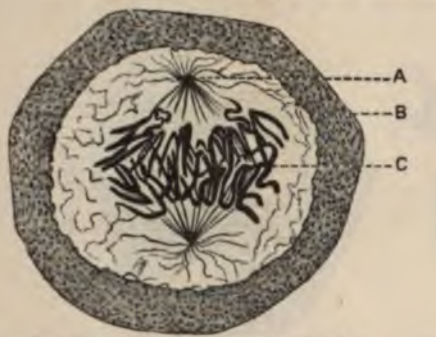

FIG. 6.—EPITHELIAL CELL OF SALAMANDER. (*Flemming.*)

A, pole and achromatine threads; B, cell-body; C, disk-like arrangement of chromatin threads at equator of nucleus.

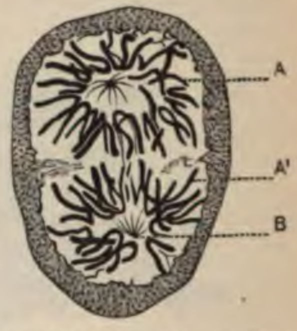

FIG. 7.—EPITHELIAL CELL OF SALAMANDER. (*Flemming.*)

A, A', chromatin threads of daughter-stars; B, achromatine threads and pole.

Phase V. The threads in the daughter-nucleus form a wreath, after which they contract more and more until the undivided convolutions can hardly be recognized.

A nuclear membrane again appears, after which the net-work returns to its quiescent state.

There is a strong tendency at the present time to refer all karyokinetic changes to the agency of the nucleus, and to ascribe to the protoplasm of the cell the passive rôle of a nutritive substance. In the impregnated ovum the influence of nuclear changes has been described, but at the same time it was shown that the protoplasm of the cell is capable of automatic as well as responsive action. Pflüger asserted that gravitation is the sole guiding agency in the process of cleavage of protoplasm. According to Born, Herturg, Weismann, and Kölliker, the protoplasm alone is isotropic, but Whitman thinks that this is far from the truth. Others, like Pflüger, believe that the protoplasm contains physiological molecules from which organs are developed. Polarity of cell-protoplasm and in nucleus exists independently, and is not reciprocal. Contractions in unfertilized ova have been observed. M. Nussbaum was the first to prove that enucleate fragments of an infusorium are incapable of reproduction, while parts of an infusorium containing a nucleus possessed this power. This would tend to establish the fact that the nucleus is indispensable to the preservation of the vegetative energy of the cell. On the other hand, Gruber, in one of his experiments, divided a stentor before fission had taken place in such a manner that the sections contained no nuclear substance, and yet the next day each one of these parts represented a complete stentor. Against the conclusions drawn from this experiment it might be urged that some of the nuclear chromatin threads might have found their way into the cell-protoplasm, and that from them the process of reproduction started. Nussbaum regards a combination of nuclear structure and cell-protoplasm as essential for cell-production. According to Flemming, the cell-body begins to divide toward the end of the fourth phase of karyokinesis. Cell-division commences with a constriction at the equator, which becomes deeper and deeper as the daughter-cells assume cell form, until complete regeneration takes place. Toward the completion of the separation only a few achromatine threads (Fig. 8, B) connect the two. To Flemming belongs the credit of having first discovered karyokinetic changes in cells undergoing division, but our knowledge of this subject has been greatly advanced by the combined labors of Strassburger, Arnold, Klebs, and Whitman. Arnold studied this method of cell-division in giant cells of the medulla and in the blood-corpuscles of leukæmic blood. He preserved the blood-corpuscles in a 6-per-cent. methyl-green salt-solution, which preserves cells in a good condition if

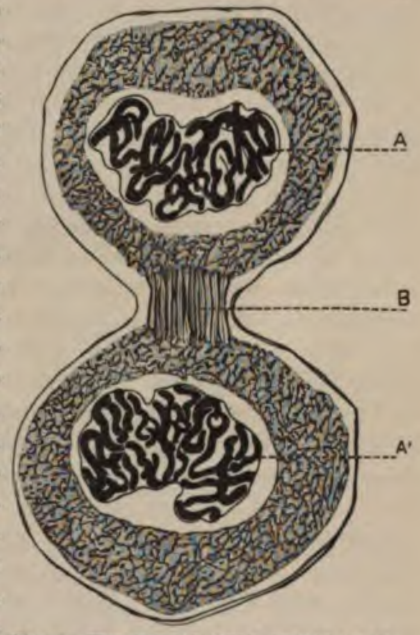

FIG. 8.—EPITHELIAL CELL OF SALAMANDER. (*Flemming.*)

A, A', daughter-glomeruli; B, achromatine threads still uniting the two daughter-cells.

the solution is kept at a proper temperature in the moist chamber on the object-glass. If to this solution a 25-per-cent. solution of chloride of gold is added, the karyokinetic figures are made clearer. In studying the process of karyokinesis in fixed tissue-cells in a state of infiltration, it is necessary to resort to the fixation and staining methods described by Flemming. The modern observers who have studied regeneration of epithelial cells have come to the conclusion that cell-division takes place almost exclusively by karyokinesis. Podwyssozki has studied this method of cell-reproduction with special reference to regeneration of liver-cells, and has come to some very important conclusions. In cats and young guinea-pigs he observed, after injury of the liver, extra-nuclear chromatin substance before he could detect any karyokinetic figures in the nucleus. The chromatin in the cell-body appeared in two forms,—either as fine granules scattered diffusely through the protoplasm of the cell, or as lumps of chromatin, and he designated these larger masses as prochromatin; but he also noticed that the granular form, at a later stage, aggregated and formed masses which united with the nuclear chromatin. Klebs explains the presence of chromatin in the cell-protoplasm to an extra-cellular origin,—the leucocytes. He believes that the chromatin contained in leucocytes is liberated after fragmentation has taken place and enters the young cells, where they serve as food and become a part of the nuclear net-work. This view is strengthened by the statement of Podwyssozki that he found numerous leucocytes in the immediate vicinity of the new cells. Ziegler and Obolensky produced arsenical intoxication in animals by administering in daily doses subcutaneously, and when they examined the liver they found well-marked karyokinetic figures in the endothelial cells of the intra-acinous capillaries, the epithelia of the bile-ducts, and, less frequently, in the secreting cells. Karyokinetic figures were first visible in the nuclei of the capillary endothelia, and were undoubtedly caused by the direct action of the arsenic upon the cells. These experiments show that karyokinesis will follow the application of chemical as well as traumatic irritants.

FRAGMENTATION OF NUCLEUS

Arnold and Pfitzner have described, in giant and other cells undergoing pathological changes, direct fragmentary division of the nucleus, by which it may break up into many parts, often of unequal size, without contemporaneous division of the cell. Arnold and others have also described incomplete fragmentation of the nucleus where the nuclear masses remain connected with each other, and can be seen as lobulated and reticulated structures. Arnold saw fragmentation of the nucleus in the cells of the marrow of bone and in leucocytes undergoing transformation into pus-corpuscles. A nucleus which undergoes fragmentation contains but little chromatin substance, and is therefore incapable of multiplication by karyokinesis; and such cells, according to the investigations of Klebs, never take an active part in the regeneration of tissue.

DIRECT CELL-DIVISION.

In 1841 Martin Barry first made the observation that the division of cells was accompanied with division of the nucleus, and for a long time it was believed that this process is simply a segmentation of the nucleus, followed by division of the whole cell. Remak taught that direct division commenced in the nucleolus, extended to the nucleus, and finally resulted in fission of the cell-body, each of the new cells containing a daughter-nucleus.

According to Pfitzner, direct cell-division is a more frequent method of cell-multiplication than the indirect in young animals where cell-proliferation is rapid. In the embryo the nucleus contains but little chromatin, and therefore the karyokinetic figures are less abundant.

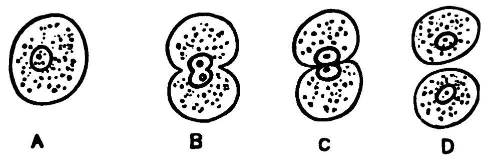

FIG. 9. (*McKendrick.*)

A, mature cell; B, commencing division of nucleus and contraction of cell-protoplasm in the centre; C, complete division of nucleus and cell; D, formation of two new cells.

In most of the regenerative processes in mature tissue-cells reproduction takes place by karyokinesis, and only in exceptional instances by direct division. The new cellular elements present karyokinetic figures in all stages, and *wherever these are seen it is a positive evidence that the fixed tissue-cells are the seat of tissue-proliferation, and that wounds are healed and defects repaired exclusively by this method of cell-formation.*

GRANULATION TISSUE.

The new cells formed by indirect or direct cell-division in a wounded or injured part, the seat of regenerative processes, constitute the granulation tissue as long as they remain in their embryonal state. As immediate union never takes place in any part or tissue of the body, we are forced to admit that every wound heals only by the interposition between the divided parts of a greater or less amount of granulation tissue. If the wound remain aseptic, and the surfaces of the wound are kept in accurate coaptation, the healing is accomplished in a short time, and by the production of a minimum amount of new tissue. A similar wound, with great loss of tissue precluding the possibility of bringing the parts in apposition by mechanical resources, must necessarily heal by the production of a large quantity of granulation tissue, the process of repair in both instances being the same, the difference being mainly the length of time required to complete the healing process and the amount of new material necessary for this purpose. In the first case the wound heals without visible granulation tissue; in the latter the defect becomes covered with granulations before the wound can heal. The macroscopical and microscopical appearances of granulating surfaces are nearly identical in all the tissues. A bone covered with granulations looks the same as a granulating surface of any of the soft tissues. Even the embryonal cells of which the granulations are covered, so long as they remain in this state, furnish, from their microscopical appearances, only remote or no indications as to their histogenetic source and ultimate destination. Differentiation takes place during their further development toward the completion of the healing process. The bulk of all granulation tissue is derived from the connective tissue as this mesoblastic structure is diffused throughout the entire body, and, with the exception of the nervous system, is found in almost every organ. In the nervous system it is

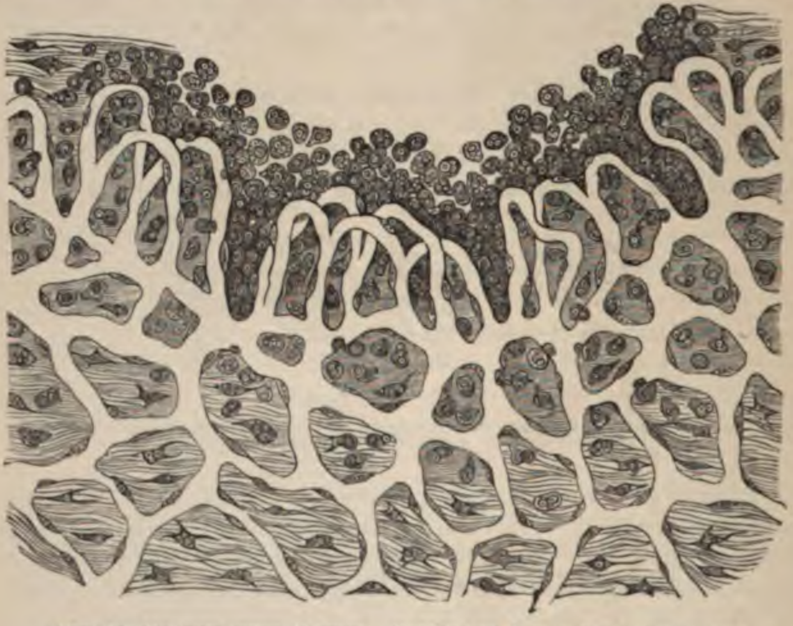

FIG. 10.—GRANULATING WOUND. CAPILLARY LOOPS SURROUNDED BY EMBRYONAL CELLS. × 300–400. (*Billroth-Winiwarter.*)

represented by an almost similar tissue,—the neuroglia,—which performs the same rôle in the repair of injuries and defects of the brain, spinal cord, and nerves. A wound or defect covered with granulations presents a velvety appearance, each tuft or papilla representing a separate loop or net-work of new capillary vessels.

The new capillary vessels are paved with endothelial cells containing a very large nucleus. Sometimes a single capillary vessel enters a papilla and gives off a number of branches, which form a net-work of convoluted vessels, rendering the granulations exceedingly vascular and liable to bleed on the slightest provocation.

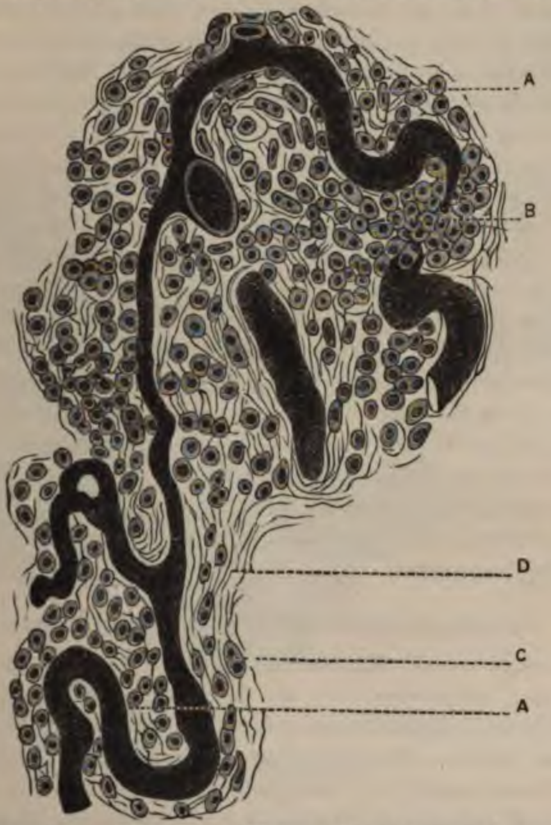

FIG. 11.—GRANULATION TISSUE FROM WOUND. BLOOD-VESSELS INJECTED. × 400. (*Hamilton.*)

A, A, capillary loops with several branches; B, ordinary granulation cells; C, fibroblasts; D, stroma.

The blood in the tuft is collected and returned usually through one vein. Emigration of leucocytes through the walls of the new capillary vessels is a common occurrence, and, when they reach the surface, form one of the elements of secretion of the wound. When the capillary vessels are imperfectly developed, or when they are in a state of inflammation, the exudation becomes profuse, and the granulation surface becomes covered with a membrane consisting of the products of coagulation necrosis. Wounds presenting such an appearance have frequently been mistaken as an evidence of diphtheritic infection. The so-called healthy granulations are small, firm, and of a pinkish-red color, and such a surface is only moistened with colorless, viscid fluid. Wounds covered with such granulations heal rapidly and leave a small, pliable cicatrix. Profuse flabby and pale granulations indicate a want of general vitality, or more frequently the presence of specific microbes, which act injuriously upon the process of transition of embryonal cells into tissue of a higher type. Such granulations are frequently met with in wounds after imperfect operations for tubercular lesions, in suppurating wounds, and in ulcers of the lower extremities, where the vascular conditions are unfavorable for the growth and development of new tissue. Histologically granulation tissue is composed of a delicate, œdematous reticulum, and upon its fibres can be seen numerous connective-tissue corpuscles. The reticulum is intimately connected with the blood-vessels, and in its meshes are contained the embryonal cells and leucocytes, the latter serving as food for the former. The embryonal connective-tissue cells are about two or three times larger than the leucocytes. The giant cells which are occasionally found are fibroblasts which have grown to such enormous proportions by inclusion of nutritive material derived from disintegrating leucocytes.

VASCULARIZATION OF GRANULATION TISSUE.

The vessels which furnish the blood-supply to the granulation tissue are new structures, and are usually formed from pre-existing vessels in injured vascular tissue, and from the nearest blood-vessels in non-vascular tissue. Vessel formation and tissue proliferation are initiated simultaneously, and keep pace with each other until the necessary amount of granulation tissue has been produced, when, during the transformation of the embryonal cells into permanent tissue, the vascular supply is gradually diminished by the obliteration and disappearance of all of the superfluous vessels. As the layer of granulation tissue seldom exceeds more than $\frac{1}{8}$ inch in thickness, the new vessels always remain short, and retain their communication with the pre-existing vessels from which they started. Travers, in his experiments on injuries of the frog's web, has observed that the blood in the divided vessels becomes stagnant some little distance from the wound. During this time material oozes from the cut vessels, which constitutes the primary-wound secretion.

Before granulations can be established the circulation must become restored by enlargement and multiplication of preformed vessels.

The capillary vessels which have been cut or otherwise injured are closed with nature's hæmostatic—a minute thrombus. The intra-vascular pressure on the proximal side of the obstruction results in dilatation of the vessel, which produces an increased blood-supply to the part commensurate with the increased demand for nutritive material. The new blood-vessels are formed by angioblasts, which are proliferated from preexisting vascular structures. Arnold has studied the formation of new blood-vessels in the stump of the tail of tadpoles after amputation, and in keratitis vasculosa artificially produced in the cornea of rabbits. To the researches of this author we owe most of the knowledge we possess on this subject. The new vessels are produced by the budding process from capillaries near the surface of the wound. The bud appears first as a circumscribed thickening of the capillary wall, which soon projects outward in the form of a triangular cellular mass composed of angioblasts. The bud is then transformed into a long string, terminating in a delicate granular thread.

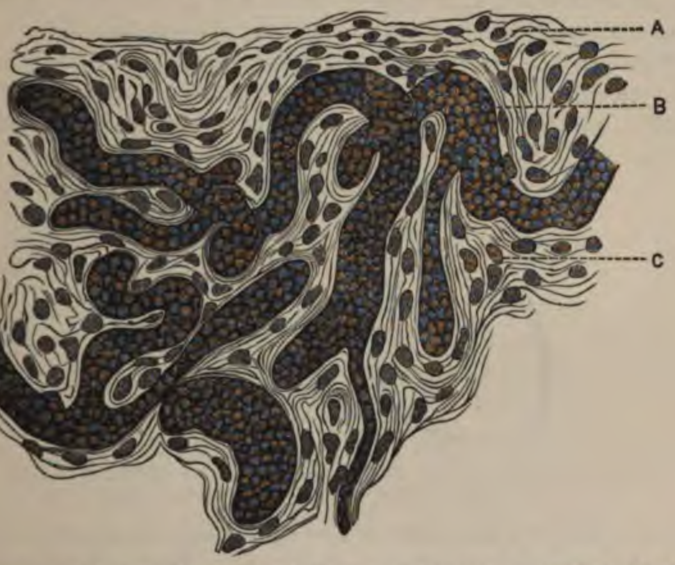

FIG. 12.—SUPERFICIAL CAPILLARIES OF A WOUND BEGINNING TO GRANULATE, ABOUT FORTY-EIGHT HOURS AFTER ITS INFLICTION. × 350. (*Hamilton.*)

A, free surface; B, the capillary loops all distended with blood, and being driven outward in tortuous festoons; C, embryonal cells.

The base of such a projection becomes excavated, and blood enters from the vessel to which it is attached. When the terminal ends of two of such projections meet they unite and form an arch, which, after they have become permeable to the blood-current, constitute a capillary loop from which branches again may develop in the same manner. The new channels contain, upon their inner surfaces, nuclei at variable distances, which subsequently undergo transformation into endothelial cells. The adventitia is formed by round cells, which arrange themselves along the outer surface of the new channels. Hunter maintained that blood-vessels are formed in granulations independently of pre-existing vessels, in the same manner as in the embryo, and that they enter into communication with the vascular system subsequently. Such a method of vascularization during post-embryonic life is not proved. A number of pathologists, and among them Billroth, still believe that blood-corpuscles and blood-vessels can be produced from connective tissue. They claim that connective-tissue cells in the intercapillary spaces enlarge, become branched, and that by union between similar projections between two or more cells hollow spaces are created which serve as blood-vessels, while the nucleus assumes the rôle of a hæmapoietic organ,—a process which is well illustrated by Fig. 14.

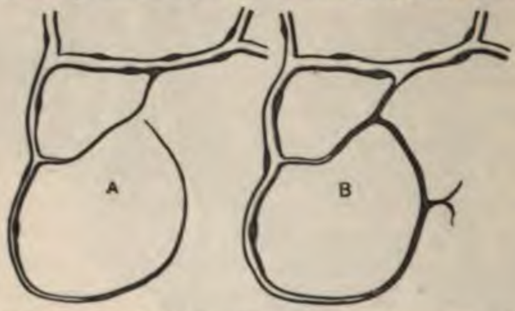

FIG. 13.—FORMATION OF NEW BLOOD-VESSELS BY BUDDING. (*Arnold.*)
A, after three hours; B, after six hours.

Still another method of vessel formation in granulations has been observed and described by Travers. He noticed that, when one of the new capillary vessels ruptures and blood is poured out into the granulation tissue, among the embryonal cells a vascular space without walls is formed. The extravasated blood, under these circumstances, did not disintegrate, and as soon as the space came in contact with another capillary loop the wall gave way and a communication was established between the two capillary vessels, and later the channel became lined with endothelial cells. This method of vessel formation is termed canalization. While the possibility of the development of new vessels independently of preformed blood-vessels cannot be denied, such an origin is, to say the least, exceedingly rare, and for all practical purposes, when we speak of vascularization of granulation tissue or the formation of new blood-vessels in general, we mean the formation of new channels by tissue proliferation from the walls of pre-existing blood-vessels. Dr. J. Hamilton, author of the excellent "Text-Book of Pathology," asserts that the blood-vessels in granulation tissue are not new, but dilated, tortuous, preformed vessels.

In wounds that heal rapidly the existence of most of the new blood-vessels is a short one. With the beginning of cicatrization they disappear rapidly, and comparatively only a few of them remain as permanent structures as a system of collateral vessels which restore indirectly the loss of continuity between the divided vessels. A failure of the vessels to disappear after cicatrization has been completed usually is an indication that some pathogenic micro-organisms have become embedded in the scar-tissue, which interfere with the proper and prompt transformation of embryonal into permanent tissue. Such scars are often met with after operations for tubercular lesions and after the healing of extensive burns, being caused in the first instance by the bacillus of tuberculosis and in the latter by pus-microbes. The vascular conditions in granulating surfaces should be carefully studied, and in the treatment due attention should be given to this important point, as compression and position are potent measures in improving a faulty circulation, which may have indefinitely retarded the healing process.

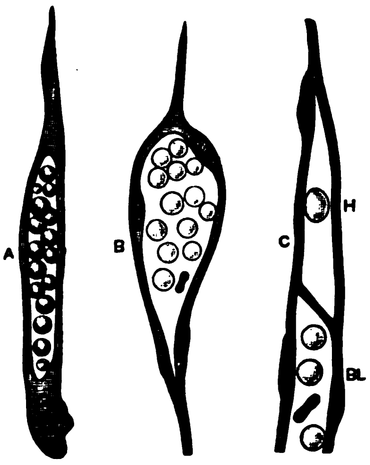

FIG. 14.—DEVELOPMENT OF BLOOD-CORPUSCLES IN CONNECTIVE-TISSUE CELLS, AND TRANSFORMATION OF THE LATTER INTO CAPILLARY BLOOD-VESSELS. (*Fluegge.*)

A, an elongated cell with a cavity in its protoplasm occupied by fluid and by blood-corpuscles; B, a hollow cell, the nucleus of which has been multiplied: the new nuclei are arranged around the wall of the cavity, the corpuscles in which have now become discoid; C, shows the mode of union of a "hæmapoietic" cell, which, in this instance, contains only one corpuscle, with the prolongation (BL) of a previously existing vessel. A, and C, from the newborn rat; B, from fœtal sheep.

CICATRIZATION.

The process of transformation of the embryonal cells in granulation tissue into permanent, fixed tissue-cells is called cicatrization. Sir James Paget has well said that during the stage of the healing process a life of eminence is changed into one of longevity. In tissues endowed with great vegetative powers and a high degree of adaptation, even large defects are replaced by tissue which resembles to perfection, anatomically, histologically, and physiologically, the injured pre-existing tissue. This is the case in injuries involving considerable loss of substance in

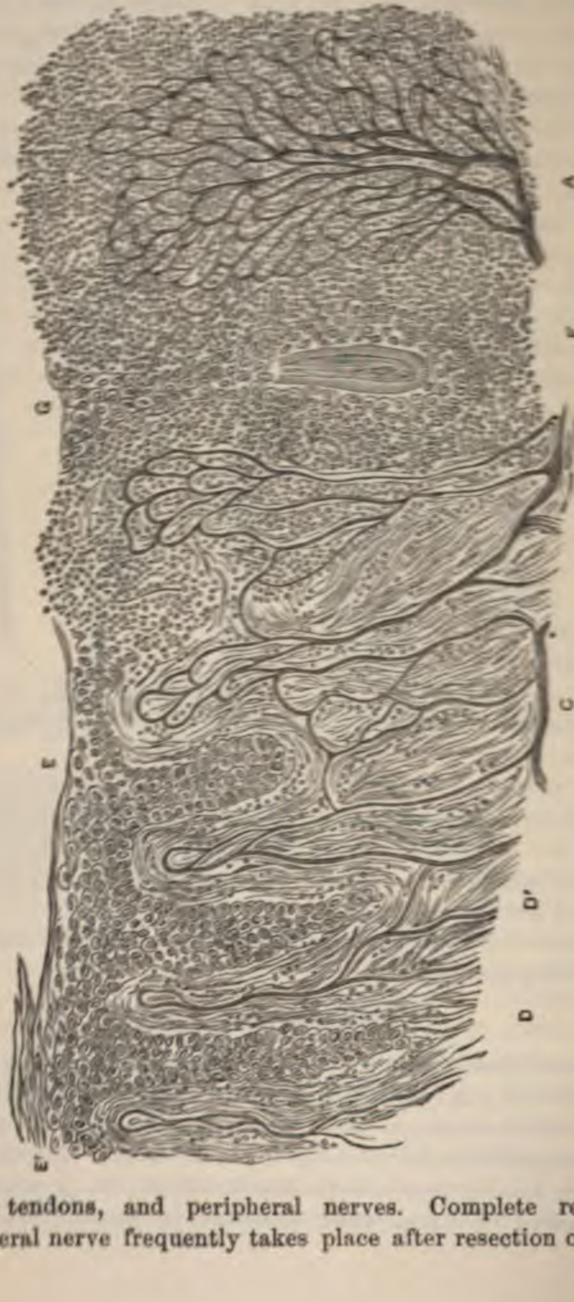

FIG. 15.—GRANULATING WOUND UNDERGOING CICATRIZATION. (*Landerer.*)

A, vessel with numerous lateral branches; granulation cells not much changed, only few spindle cells near the main trunk; B, cicatrization further advanced; spindle cells predominate; C, D, D', cicatrization well advanced; E, E', epithelial cells; F, hair-follicle with proliferation of epithelial cells in its interior, new cells reaching the surface, G.

bone, tendons, and peripheral nerves. Complete restoration of a peripheral nerve frequently takes place after resection of more than an inch of its continuity. In subcutaneous tenotomy the tendon-ends may be kept separated for two or more inches, and yet after a few months it would be difficult to ascertain, even after the most careful examination, the site of operation. The fractured ends of a broken bone may be completely separated by lateral displacement during the entire time required in the healing process, and yet they are firmly united by the interposition of a connecting bridge of new bone. In other tissues endowed with less reparative energy, as for instance the muscular fibre, a slight separation results in the formation of cicatricial tissue between the anatomical structure which it is the intention to unite. By cicatrization is therefore understood the completion of the reparative process, and the term does not necessarily imply the formation of a permanent cicatrix. An ideal healing culminates in the formation of tissue which effects a physiological restitution of a defect caused by injury or disease. As a rule, it can be stated that the result will be satisfactory in proportion to the amount of granulation tissue produced or required in the process of repair. In an aseptic wound the reparative material will not be in excess of the local demand, and the demand will depend on the degree of accuracy of approximation of the surfaces of the wound. Cicatrization begins in the granulation tissue nearest the preformed vessels; that is, the margins and surface of the wound.

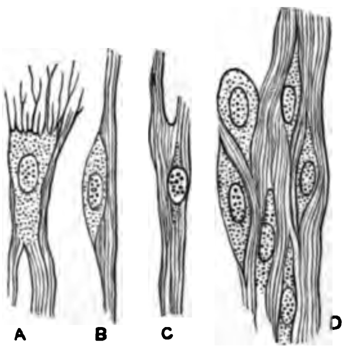

FIG. 16.—EMBRYONAL CONNECTIVE-TISSUE CELL UNDERGOING TRANSFORMATION INTO MATURE STATE. (*Ziegler.*)

A, the cell-body; still contains a considerable amount of protoplasm, which, however, gradually diminishes toward D, where it represents a mature connective-tissue cell with a very small amount of protoplasm surrounded by connective-tissue fibres.

The embryonal connective-tissue cells, or fibroblasts, as they are called, at first round, become elongated with thread-like prolongations from the extremities.

The new connective tissue contracts, thus bringing the margins of the wound or granulating surface in closer apposition, and by its constricting effect assisting in the obliteration of superfluous vessels. The cicatrix or scar will be large if the process of granulation has been in excess of the demand, or if a large defect had to be healed by the deposition or interposition of a large quantity of cicatricial material. Large scars should be prevented, if possible, by appropriate treatment, as from the contraction they give rise to distressing deformities, and from their low vitality they furnish a permanent predisposition to ulcerative processes and not infrequently become the seat of malignant disease. After the healing of any ulcer of considerable size upon the mucous surface of any of the hollow viscera the cicatricial contraction often gives rise to the formation of strictures. Nerves appear to form in granulations, as these are often exceedingly tender to the touch. Their existence, however, has not been demonstrated. The pain and tenderness may be caused by force being transmitted to subjacent nerves. According to Vanderkolk, no lymphatic vessels are present in granulation tissue. During the process of cicatrization all the embryonal cell-elements undergo transformation into mature tissue, the fibroblasts are converted into connective tissue, the angioblasts into vessels, the myoblasts into muscle-fibres, the osteoblasts into bone, etc., each histological element represented in the wound or defect furnishing the material for its own repair.

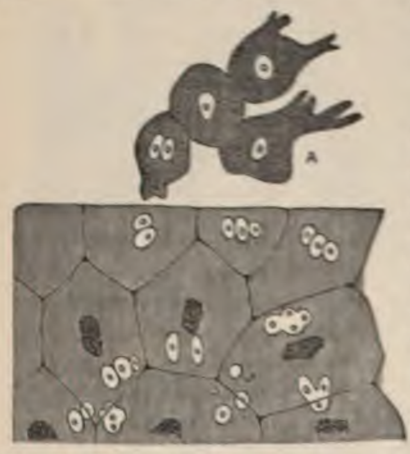

FIG. 17.—WANDERING EPITHELIAL CELLS FROM FROG. (*Klebs.*)

A, old epithelial cells upon edge of wound of skin, with proliferation of nucleus.

EPIDERMIZATION.

A wound of the external surface of the body can be said to have healed after the completion of epidermization. In accordance with the general law of succession of cells, epidermization takes place exclusively by proliferation of preformed epithelial cells. The new epithelial cells have a more or less rounded shape, and cover the granulations from the margins of the wound, where the new skin appears as a bluish-pink pellicle. At first they do not readily adhere to the granulations, but appear to cover them (Fig. 15, E′); later, however, they throw down long processes which penetrate the granulations, and in this way obtain a permanent foothold. New epithelial cells possess amœboid movements, may become detached from the epithelial matrix, and wander some distance and form permanent attachments, and in such an event an independent centre of epidermization is established. Migration of epithelial cells was first observed and described by Klebs in superficial wounds in the skin of the frog.

The irregular projections of the new skin over the granulations, so frequently observed during the healing of wounds by granulation, is undoubtedly often due to such a displacement of embryonal epithelial cells. In granulating surfaces following destruction of the skin by burns, caustics, or ulceration, independent centres of epidermization are often seen in the midst of the field of granulations. In such cases the entire thickness of the skin at some points has not been destroyed, and epithelial proliferation takes place from remaining remnants of glands, as is well shown at F and G in Fig. 15. The granulations in the immediate vicinity of the zone of epidermization become reduced in size, the blood-vessels are diminished in number, and the subjacent fibroblasts are rapidly converted into connective tissue. In wounds of the skin which heal without visible granulations the papillæ are absent from the cicatrix, even although it be broad from subsequent yielding to traction. In wounds healing by open granulations new papillæ are formed in the new skin, because the capillary loops atrophy downward and become the papillary vessels. Epidermization and cicatrization are favorably influenced by measures which secure for the wound an aseptic condition throughout, and by keeping the delicate granulations covered with protective silk until the wound is completely healed.

POSITIVE INDICATIONS IN THE TREATMENT OF WOUNDS, WITH SPECIAL REFERENCE TO SECURE UNION BY FIRST INTENTION.

Absolute Asepsis.—*Absolute asepsis can only be secured by strictest antiseptic measures. Surgical cleanliness is more than ordinary cleanliness.*

Antiseptic precautions are employed for the purpose of securing for the wound and everything that is brought in contact with it an aseptic condition. The mechanical removal of microbes from the field of operation by shaving and washing with warm water and potash-soap should be as thorough as possible, but cannot be relied upon in securing asepsis. The surface must be disinfected with a reliable germicidal solution, either a 1-to-1000 solution of corrosive sublimate or a 4-per-cent. solution of carbolic acid. Accidental wounds must always be considered as infected wounds, and a faithful effort must be made to render them aseptic by exposing, if possible, the entire wounded surface to the direct action of one of these solutions, while the surface for a considerable distance around it is also disinfected. Recently, a weak solution of the double cyanide of mercury and zinc has been recommended by Sir Joseph Lister as an antiseptic, and, from his experimental investigations and clinical experience, it appears that this substance possesses an advantage over carbolic acid, corrosive sublimate, and other antiseptics, as it exerts an inhibitory effect upon microbes which still may remain in the wound or its immediate vicinity, which prevents them from multiplying in the tissues or in the dressing. The hands of the operator and his assistants are to be cleansed by washing in warm water and potash-soap, and then disinfected in a 1-to-1000 sublimate solution, and, lastly, washing in absolute alcohol. Special care is to be exercised in cleansing and disinfecting the space under the finger-nails. On each side of the wound or field of operation a towel wrung out of an antiseptic solution is spread smoothly, in order that, during the operation, instruments and sponges will not be contaminated by being brought in contact with non-aseptic clothing or surface. None but sterilized sponges are to be used, and, in the absence of such, pieces of aseptic gauze, folded into convenient shape, should be used as substitutes. The cheapest and most reliable method of disinfection of instruments is to boil them for five minutes and then place them upon an aseptic towel, ready for use. If these antiseptic precautions have been faithfully carried out, sterilized water can be used for irrigation during the operation, or the dry method of operating recently introduced into practice by Landerer can be followed in operating upon aseptic tissues or in the treatment of aseptic wounds. In the operative treatment of suppurative affections, irrigation with a 1-to-5000 solution of sublimate must be frequently resorted to during the operation, and, in the removal of tubercular products, irrigation with an aqueous solution of the tincture of iodine, made by adding enough of the tincture to sterilized water to impart to the solution a sherry color, should be used.

CAREFUL HÆMOSTASIS.

The presence of a blood-clot between the surfaces of the wound is objectionable for the following reasons: 1. It separates mechanically the surfaces which it is intended to unite. 2. It serves as a culture medium for micro-organisms, which, if in contact with living tissue, might remain harmless. 3. It gives rise to tension, and consequently becomes productive of pain and an undue degree of reflex irritation. For years, von Bergmann has insisted that careful arrest of hæmorrhage is one of the most urgent and important indications in the treatment of wounds, and his teachings merit the attention of every prudent surgeon. Bleeding points should be tied with sterilized catgut or silk. A number of surgeons have discarded catgut, as it is more difficult to render it aseptic than silk. The latter can be readily sterilized by boiling. The hæmorrhage that so often interferes with an ideal healing of the wound is the capillary or parenchymatous oozing, and this should always be carefully arrested before the wound is sutured. The following measures should be resorted to in controlling this form of bleeding, and in the order named: 1. Position. 2. Surface compression. 3. Hot-water irrigation. 4. Antiseptic tampon.

1. In wounds of the extremities, capillary oozing is usually promptly arrested by holding the limb in a perpendicular position. In this position the intra-arterial pressure is diminished and the return of venous blood

favored, both of which are important elements in diminishing the amount of blood in the capillary vessels. In order to produce the desired effect, this position should be maintained for fifteen to twenty minutes, and the limb should be kept in this position for at least six hours after the operation.

2. Surface pressure with a flat sponge or a compress mechanically arrests the bleeding, and the capillary vessels, partly or completely emptied of blood, are placed in a more favorable condition for the formation of a thrombus. After an amputation, for instance, the sponge or compress is applied to the surface of the cut muscles and the flaps are laid over it, and compression with two hands applied, with the limb in a perpendicular position before the elastic constrictor is removed. Compression, continued in this manner for ten or fifteen minutes, will usually be successful in completely arresting parenchymatous bleeding.

3. Irrigation with water at a temperature sufficiently high to coagulate the albumen on the surface of the wound seals mechanically the cut vessels, and, at the same time, produces a localized anæmia by contracting the terminal arterial branches. A temperature of 120° F. will answer for this purpose.

4. Styptics should never be employed in arresting bleeding from a recent wound. If the procedures mentioned fail in accomplishing the desired object, the wound should not be sutured until hæmorrhage has been completely checked by the use of the antiseptic tampon. The wound is packed with iodoform gauze, and the customary dressing is applied in such a manner as to exercise uniform gentle pressure. After twenty-four hours the dressing and tampon are removed, and the wound closed with sutures. In such cases secondary suturing is of great value in securing a speedy and satisfactory healing of the wound.

ACCURATE SUTURING.

Brilliant operators are not always the best surgeons. The best results in surgery follow the one who is most painstaking in following out the minutest details. This assertion applies most forcibly in the treatment of wounds. The surgeon here occupies the position of handmaid to the *vis medicatrix naturæ*, and in the exercise of his duties must do all in his power to tax only to a minimum extent the regenerative resources of the wounded tissues. In the treatment of wounds it becomes his imperative duty, not only to unite the surfaces of the wound accurately and neatly, but to unite, whenever it becomes necessary, tissues of the same anatomical structure and physiological function. Divided nerves, tendons, muscles, fascia, must be separately united with buried sutures before the wound is closed by the ordinary interrupted or continuous suture. When several nerves or tendons have been divided in the same wound, great care must be exercised to unite the ends of the same nerve or tendon. Accurate approximation of a deep wound is impossible without the buried suture. Several rows of these sutures may be required. Reliable catgut should be preferred for the deep sutures, but if this material is not at hand fine silk can be used. The best materials for the ordinary interrupted sutures are silk or silk-worm gut. Separate sutures for the skin are usually required in order to approximate the superficial margins of the wound accurately. If the surgeon has reason to believe that the wound is aseptic, drainage should be dispensed with, because the manner of suturing, as just described, guards against the occurrence of "dead spaces." An absorbent antiseptic compress, composed of a few layers of iodoform gauze and a thick layer of salicylated cotton, or sublimated moss or wood-wool, is the most appropriate dressing for such cases. The bandage to retain this dressing is applied in such manner as to exercise uniform equable compression,—an important element in affording support to the injured vessels and in securing rest for the parts involved in the injury.

PHYSIOLOGICAL REST.

In the after-treatment of a wound nothing is more important than to secure for the parts which have been mechanically united, as far as possible, physiological rest. The importance of rest in the prevention and treatment of inflammation has been prominently brought forward by Hilton, and his teachings have resulted in a great deal of good in the treatment of inflammatory surgical affections. If one of the extremities is the seat of the wound, immobilization upon a splint or with a plaster-of-Paris dressing, in such a position as to relax the muscles involved in the wound, is of paramount importance. The injured part must be kept in a position which will favor a normal blood-supply and prevent passive hyperæmia. A wound properly dressed should not be disturbed until union has taken place. If any one of the three most important indications for a change of dressing—pain, rise in temperature, and saturation of the dressing with wound-secretions—do not arise, the first dressing is allowed to remain for eight days to six weeks, according to the location, character, or size of the wound. In wounds of the gastro-intestinal canal, physiological rest is secured by abstinence from food, and, if necessary, peristalsis is diminished by a few doses of opium. In wounds of the bladder distention of the organ is prevented by the introduction and retention of a catheter. In wounds of the brain or its envelopes, rest is secured by exclusion of light and by enforcing quietude in the patient's room.

UNION BY SECONDARY INTENTION.

In an aseptic wound all the new material resulting from proliferation of the fixed tissue-cells is used in the process of repair, and the time for healing of the wound will depend on the anatomical structure of the part injured and the amount of material required to form a bridge of living tissue between the divided parts. As long as the wound heals without destruction of any of the new tissue-elements by specific microbic causes, it is proper to speak of a union by primary intention, whether the healing is completed in three or four days, or whether it is protracted for months until the ultimate object of wound treatment has been reached. From a pathological, and even from a practical, standpoint, it is not correct to include, under the head of healing by the second intention, aseptic wounds that, on account of want of proper approximation, or on account of loss of tissue, have of necessity to heal by granulation, with infected wounds in which the regenerative processes are disturbed by suppuration. In a suppurating wound the embryonal cells which are destined to become transformed into new tissue are exposed to the destructive action of pus-microbes and their ptomaines, their protoplasm is destroyed, and they become one of the histological sources of pus-corpuscles. The cells on the surface of the wound, being most distant from the vascular supply, possess the least power of resistance to the action of pus-microbes, and on this account, as well as from the greater number of pus-microbes on the surface of the wound than in the deeper tissues, they are converted into pus-corpuscles. As long as suppuration remains active the superficial layer of granulation cells are destroyed, and as soon as other embryonal cells take their place the process is repeated, and thus the healing of the wound is indefinitely delayed.

When a favorable change takes place in the wound, either spontaneously or from the employment of antiseptic measures, suppuration is diminished, the granulations become firmer and more vascular, and cicatrization and epidermization now progress in a satisfactory manner. Such a favorable change in the condition of the wound can be readily explained after the use of such agents as are known to destroy the microbic cause of the suppuration when brought in contact with the wound. In such a case we would naturally expect that, with the removal, destruction, or rendering inert of the pus-microbes, the embryonal cells would remain attached to the point where they were produced, and would soon be converted into tissue resembling the matrix which produced them. Spontaneous cessation of suppuration, and with it the conversion of a surface covered with dead material into a healthy granulating surface, would indicate either that the virulence of the pus-microbes had become attenuated, that the soil was no longer congenial for their multiplication, or finally that the resistance on the part of the tissues to their pathogenic action had become increased. That tissue resistance has a potent influence in neutralizing and modifying the action of pathogenic micro-organisms has been observed clinically and demonstrated experimentally. Suppurating wounds are graver affections, and are more difficult to manage in the aged and in badly-nourished persons, as well as in patients debilitated from excesses and other protracted diseases. A good circulation of the part is an important element in counteracting the cause of suppuration. A chronic varicose ulcer of the leg that suppurates freely, as long as the patient continues to use the limb, is often transformed into a healthy granulation surface after a few days of rest in bed, with the affected limb in an elevated position.

TREATMENT OF SUPPURATING WOUNDS, WITH SPECIAL REFERENCE TO HASTENING THE PROCESS OF REPAIR.

In the treatment of an accidental wound, which always must be regarded as a septic wound, or in the management of a wound where the antiseptic precautions have failed, no time should be lost in securing for the wound and its vicinity an aseptic condition by thorough disinfection. The surroundings of the wound are disinfected in the same manner as for an operation. The wound is exposed as thoroughly as possible to direct treatment by enlarging it over recesses otherwise inaccessible, after which it is thoroughly irrigated with a solution of sublimate (1 to 2000). If the granulations are copious and flabby they must be removed with Volkmann's sharp spoon, and after the bleeding has ceased a 12 per-cent. solution of chloride of zinc is applied; after a few minutes the surplus fluid is washed away by irrigation with the sublimate solution. The wound is now dried, sutured, and drained. Drainage in these cases is a necessary evil, as the surgeon can never feel certain that he has succeeded in obtaining perfect asepsis. If the wound is extensive, or if pus has been burrowing in different directions along the deep tissues, as in cases of compound fracture where a thorough disinfection of every part of the wound, as described above, is impossible or impracticable, constant irrigation with a saturated solution of acetate of aluminum should be instituted and continued until the wound has been rendered aseptic. Acetate of aluminum is a reliable antiseptic, is non-toxic, and penetrates the tissues deeply. The treatment most appropriate for a recent aseptic wound is to be adopted as soon as suppuration has ceased and the general symptoms at the same time point to an aseptic condition.

SUTURING OF GRANULATING WOUNDS.

If union by primary intention has failed to take place for any reason in wounds which can be closed by suturing, a second attempt can be made to approximate the surfaces with sutures with fair prospects of success as soon as the granulations are in an aseptic condition. Aseptic granulating surfaces when brought in contact unite rapidly, as vascular connections between the new capillary loops are established in a remarkably short time, and the wound then heals in the same manner as after primary suturing. The cases best adapted for secondary suturing are those where suppuration has ceased, the granulations have become small and firm,—in short, wounds in which cicatrization has commenced. The *technique* in the treatment of such wounds is the same as in cases of aseptic recent wounds. The advantages of this method of dealing with wounds that have failed to unite are pronounced when the wound is deep and the margins can be coaptated without much tension. Buried sutures can be used for the same purpose and with the same benefit as in the treatment of recent wounds. Before the surfaces are brought in contact with the sutures it is important to disinfect and dry the granulations thoroughly. As secondary suturing is applicable only in the treatment of such wounds where we have every reason to assume that an aseptic condition exists, or can be secured by disinfection, the whole wound should be carefully closed and drainage must be dispensed with, in order to obtain rapid healing of the entire wound. It has been recently suggested by Kahn that in extensive defects of the skin a covering for the wound can be obtained by sliding of the skin, after undermining it for some distance in a direction most suitable. That this procedure is applicable only under circumstances when the surgeon is sure of asepsis is to be taken for granted, as otherwise it might be followed by gangrene and still greater loss of tissue.

CHAPTER II.

REGENERATION OF DIFFERENT TISSUES.

IN connection with the subject of healing of wounds it is very important for the student to familiarize himself with the vegetative capacity of the different tissues of the body in order to estimate with some degree of accuracy the part taken by each tissue in the reparative processes which take place after an injury or disease. *No positive proof has yet been furnished that the leucocytes or any other of the cellular elements of the blood take any active part in the restoration of lost parts.* It does not appear to me reasonable or logical that such an indifferent cell as the leucocyte should ever become transformed directly into a fixed tissue-cell, and it is still more improbable that it should be possessed with such a diverse vegetative capacity as to undergo a transition in one place into a connective-tissue cell, in another into bone, and still another into a muscle-fibre. It is much more rational to assume, in the repair of an injury and in the regeneration of a part destroyed by disease, that the universal law of legitimate succession of cells asserts itself, according to which the reparative process is initiated and completed by homologous cell proliferation.

In the following pages experimental and clinical proofs will be advanced which will at least tend to establish the truth of this assertion.

NON-VASCULAR TISSUE.

The part taken by blood-vessels in regenerative processes is well shown in the healing of wounds of non-vascular tissue. Large wounds of the cornea and cartilage can only heal after a blood-supply has been established through new vessels from the nearest vascular district. Rapid vascularization of the non-vascular tissues is always observed when the wound has become infected.

Cornea.—The normal cornea contains no blood-vessels, but vascular spaces, which form a system of channels for the circulation of the plasma-fluid. In 1863 Recklinghausen discovered in these spaces migrating corpuscles, resembling in size and shape the white blood-corpuscle, which he regarded as offsprings of the corneal corpuscles. Later, Cohnheim showed that these wandering cells were leucocytes which had escaped from the pericorneal capillary vessels and had found their way into these channels. In traumatic keratitis these spaces become blocked with leucocytes, and they constitute largely the primary product of inflammatory exudation long before the fixed cells of the cornea could have yielded such an amount of cellular elements. Strube and His studied experimentally the healing of wounds of the cornea and traumatic keratitis. They injured the cornea of rabbits by cutting and cauterization. As the cornea is freely supplied with nerves, they observed as one of the earliest tissue changes a reflex paretic dilatation of the marginal blood-vessels. The marginal hyperæmia was followed by the formation of new blood-vessels in the direction of the seat of injury. The early opacity around the wound and the space between the wound and the advancing channels are caused by the presence of leucocytes in the vascular spaces; later, to proliferation of the corneal corpuscles. That leucocytes enter the plasma-canals when the cornea is irritated has been definitely settled by Cohnheim by one of his most ingenious experiments. He injected finely-divided carmine suspended in an acid, or precipitated aniline into the dorsal lymph-sacs of frogs, with the result that when he irritated the cornea, a few days later, leucocytes stained with the pigment-material appeared at the margin of the cornea where cell-migration was known to appear first. He found a rapid increase of corneal corpuscles in the animal subjected to experimentation; thus, in one instance, eighteen hours after the injury, he found, in spaces normally occupied by one corpuscle, as many as 20 to 30 young cells closely packed together.

Hamilton regards as the first change in an irritated cornea an increase of the plasma-current which may destroy the endothelial lining of the canals, and according to this observer cell-migration into the corneal spaces occurs later. Unimpaired innervation of the cornea is an important factor in the prompt healing of wounds of this structure, as it is well known that in patients suffering from glaucoma, and in the aged, wounds of the cornea heal often in a very unsatisfactory manner. An aseptic wound of a normal cornea heals without opacity; the new corneal corpuscles, after they attain maturity, transmit light as perfectly as the cells from which they are produced. Imperfect restoration of tissue is to be expected when the regenerative process is complicated by a suppurative inflammation with considerable destruction of tissue. Gussenbauer incised the cornea in rabbits half-way between the centre and its margin to the extent of half a line to a line, and found, in examining the specimens after twenty-four hours, that no union had taken place. The wound-surfaces at this time were glued together by an interposed substance. The surfaces of the wound were in close contact at a point corresponding to the middle portion of the cornea, and the gap widened toward each of its surfaces so that the temporary cement-substance represented two cones with their apices directed toward each other and the bases toward the surfaces. On staining the specimens with chloride of gold it was found that this substance contained cells which were most numerous toward the surfaces of the cornea. The corneal corpuscles on the cut surfaces were seen to be enlarged and presenting different stages of cell-division. Instead of round the corpuscles were spindle-shaped, some containing one nucleus, others two nuclei; intercellular substance granular. In specimens eight days old the space between the cut surfaces was occupied almost exclusively by new corneal corpuscles, and the edges of the wound could no longer be clearly defined. During cicatrization of the wound the number of cells is diminished, while in form and size they resemble more and more the mature corneal corpuscles from which they were derived.

In a non-penetrating incised wound of the cornea the gap is filled up after a few days with young cells derived from the cylindrical cells of the deepest layer of the corneal epithelia.

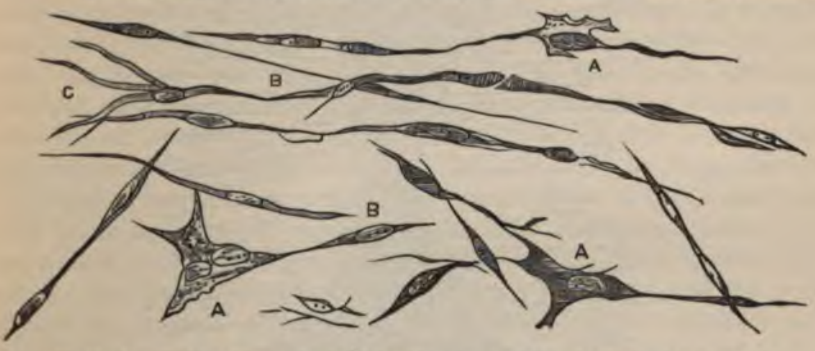

FIG. 18.—CORNEAL CORPUSCLES IN A STATE OF PROLIFERATION. (*Senftleben.*)
A, old corneal corpuscles with one or two nuclei and young offshoots, B and C.

If the wound has penetrated, the posterior third of the wound gaps toward the anterior chamber of the eye, and is first plugged with the products of coagulation necrosis, which is later replaced by epithelial cells from the membrana Descemeti (Fig. 19, C), while the anterior portion is occupied by epithelial cells the same as in the non-penetrating wounds. At the end of the first week the corneal corpuscles begin to proliferate, and the cells from this source gradually displace the epithelial cells and bring about the definitive healing of the wound. As wounds of the cornea are not sutured, the surgeon should aim to secure approximation by removing coagulated blood if present, and by correcting any displacements which may be present by direct measures, and finally by applying a dressing which will exert uniform and equable elastic compression.

Although the antiseptic treatment cannot be carried out with the same precision in the treatment of wounds of the cornea as in other localities, it is at least the duty of the surgeon to use only sterilized instruments and aseptic sponges, and to employ such mild antiseptic solutions as will at least exercise an inhibitory influence upon pathogenic micro-organisms that may be present in the wound or upon the surface of the eye.

Cartilage.—Cartilage is in every sense of the word a non-vascular structure, as even the plasma-channels found in the cornea are absent here. Plasma diffusion must take place between or through the cells. It is undoubtedly on account of the limited provisions for nutritive supply that the vegetative capacity of this tissue is so exceedingly low. Normal cartilage when injured is unable to repair the defect. The process of healing of wounds of cartilage was first studied experimentally by Redfern. In one experiment he found the wound almost unchanged after twenty-nine days. In one specimen, where the healing process had been completed, he found the defect repaired by connective tissue. The microscopical description of the healing process corresponded with that given by Goodsir of inflammatory processes in this structure. Along the margins

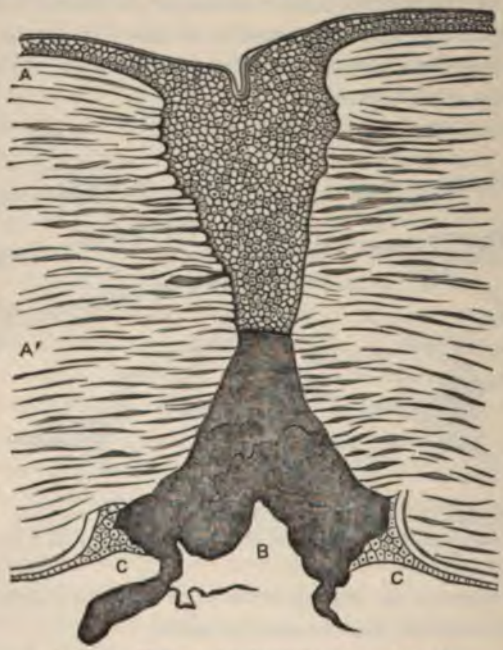

FIG. 19.—WOUND OF CORNEA. (*von Wyss.*)

A-A', new corneal corpuscles; B-A', temporary plug of fibrin; C, epithelia from membrana Descemeti.

of the wound the cartilage-cells multiply and the cement-substance is dissolved. No new cartilage-cells are produced, and the space is occupied by connective tissue. Vascularization toward the seat of injury from the marginal vessels of the perichondrium takes place in the same manner as in the cornea. Reitz traced the formation of connective tissue from the cartilage-cells in tracheotomy wounds in rabbits. He observed, after the cement-substance had become dissolved, that the cartilage-cells were transformed into spindle-cells, and later into connective tissue. He found the gap between the divided cartilage-ring filled with such cells a few days after the wound had been inflicted, and explains the discrepancy between the results he obtained and those described by Redfern on the ground of the close proximity of vascular supply in his case and the remoteness of vessels from the wound studied by Redfern, as the latter experimented on articular cartilage. Gussenbauer studied the repair of cartilage wounds after incising subcutaneously costal cartilage. In wounds twenty-four hours old a triangular gap was found filled with fibrin and blood-corpuscles. No change was found at this time in the cartilage-cells and cement-substance. The cells of the perichondrium increased in volume and changed in form. Gussenbauer was unable to verify the observation made by Reitz in wounds of trachea, that cartilage-cells are transformed into connective-tissue cells, and believes that the ammonia used by Reitz to provoke croupous pneumonia, by its introduction into the bronchial tubes through the tracheal wound, may have modified the result. He traces tissue proliferation almost exclusively to the perichondrium, the cells of which were found in all stages of division and development, while only a few of the cartilage-cells presented evidences of segmentation. Dörner studied not only the manner of repair of simple incised wounds of cartilage, but also produced more complicated injuries, and invariably found that the perichondrium took a more active part in the process of healing than the cartilage-cells. Wounds of fibro- and reticulated cartilage heal in the same manner as wounds of hyaline cartilage. The histological changes observed by Redfern, Dörner, and Gussenbauer during the repair of wounds of cartilage are descriptive of the changes which attend chondritis.

VASCULAR TISSUE.

The healing of wounds of vascular tissue is accomplished more rapidly than of non-vascular tissue, as the primary wound-secretion, which is derived mostly from the wounded vessels, forms a temporary cement-substance which glues the parts together,—a condition which renders material assistance in maintaining coaptation,—while the direct blood-supply to the injured part cannot fail in increasing the vegetative capacity of the cells, and, lastly, the leucocytes present in the recent wound serve as food for the cells which are undergoing karyokinetic changes. As a rule, to which there are few exceptions, it may be stated that the rapidity with which the healing process is completed is proportionate to the vascularity of the wounded part. For instance, wounds of the fingers heal much more rapidly than wounds of the arm or forearm, and wounds of the face more rapidly than wounds of the neck. *Karyomitotic changes are first noticed in the nuclei of cells in close proximity to blood-vessels.* In studying the healing of wounds of vascular tissue, Graser noticed that the connective-tissue cells a little distance from the surface of the wound were first to show evidences of karyokinetic changes; hence, it is apparent that the reparative process is initiated in cells most favorably located in reference to an abundant blood-supply, which corresponds to the location of capillary vessels which are undergoing dilatation prior to the formation of new blood-vessels. Regeneration of tissue takes place most rapidly in parts where new blood-vessels are developed early, rapidly, and abundantly. The healing process is retarded or completely suspended when the capillary vessels, new and old, are seriously altered by inflammation.

Surface Epithelia.—Epithelial cells in a normal condition receive no direct blood-supply, but their relations to the subjacent vascular tissue are so intimate, and their proliferation in the healing of surface wounds and in the repair of defects caused by pathological conditions is so largely dependent on the development of new blood-vessels, that the study of their regeneration among the vascular tissues appears appropriate. In the consideration of this subject of epidermization, it has been shown that epithelial cells are derived exclusively from an epithelial matrix, either from the margin of the wound or an islet of the epiblast buried among the granulations. Regeneration of epithelial cells of the hypoblast takes place in a similar manner as has been described in epidermization of a wound of the cutaneous surface. Of special interest is the rapid regeneration of the gastro-intestinal mucous membrane. A recent gastric or intestinal ulcer presents elevated and swollen margins, and as long as this condition remains the healing process fails to become established until the swelling subsides, and paving of the granulations with epithelial cells is postponed until the surface of the ulcer is nearly on the same level with the surrounding border of the mucous membrane. Griffini and Vassale made gastric fistulæ in dogs for the purpose of studying directly, and during the life of the animals, the process of repair of wounds of the mucous membrane of the stomach. Through the fistula they made superficial wounds of the inner surface of the organ, and from their observations they satisfied themselves that healing takes place rapidly, and that regeneration of epithelial cells occurs in the peptic glands, where even as early as the third day the epithelial cells showed evidences of active proliferation. The new epithelial cells spread over the interglandular spaces, while a part of the glandular structure is lost during the process of healing. In traumatic defects where the glands have been excised with the mucous membrane the epithelial covering of the granulating surface is derived from the preformed epithelial cells of the mucous membrane bordering the wound. At a later stage new glands are formed by karyomitotic cellular changes after the normal type of development of glands in the embryo. Even the youngest glands have an outlet, and the structure increases in depth by extension of mitotic changes in that direction. Pepsin-secreting cells are found only after the glands have attained nearly their normal depth. In one instance they were found only partly developed on the fortieth day. Connective-tissue proliferation takes no essential part in the growth and development of the new glands. Visceral wounds of the stomach heal kindly and rapidly. Even gunshot wounds of this organ, when made with a small bullet, may heal without surgical interference, more especially if at the time the injury has been inflicted the stomach is empty and all food is withheld for a few days. A strict diet is important in the treatment of wounds or ulcers of the stomach, as Leube has obtained excellent results from treatment of chronic ulcers of this organ by an exclusive milk diet. Griffini also made the observation that the traumatic defects which he produced in the interior of the stomach of dogs healed most rapidly when food was withheld entirely for a few days, and later on nothing but milk was allowed. From these observations and experiments it is evident that the young cells are unfavorably affected by the action of the gastric juice.

Quincke has demonstrated experimentally, which has been a long-known and familiar clinical fact, that anæmia retards regeneration of the gastro-intestinal mucous membrane. In two dogs a gastric fistula was made, and through it a defect of the mucous lining was made of the same size in both animals. One of the animals was in perfect health, and healing was completed in eighteen days. The other dog was anæmic, and the healing process was prolonged thirty-one days. In the healing of an ulcer of the stomach or any portion of the intestinal canal the epithelial cells are first to take an active part in establishing a process of repair, the connective-tissue cells entering later upon their part of tissue production. The healing process terminates most satisfactorily when only a small amount of connective tissue is formed and the epithelial covering is completed in a short time, as such a scar represents almost to perfection the normal tissue it has replaced. If a large quantity of granulation tissue is produced by the connective tissue, and the formation of the epithelial covering is delayed for a long time, or is imperfectly accomplished, there is great danger of subsequent cicatricial contraction of the new tissue producing a stricture. The best possible prophylactic means against the occurrence of strictures under such circumstances are such dietetic and therapeutic measures as will secure for the ulcerated or wounded surface such favorable conditions as will expedite the paving of the surface with epithelial cells and limit the production of cicatricial tissue.

TRANSPLANTATION OF SKIN.

Epidermization of a large granulation surface is a slow process, even under the most favorable circumstances, and the resulting cicatrix is often large, gives rise to contractions, and not infrequently becomes the seat of keloid or ulcerative processes subsequently. Modern surgery offers means by which this tedious process can be materially shortened, and healing is accomplished by the formation of a more satisfactory scar.

Skin-grafting to Expedite the Healing of Granulating Surfaces.—In 1870 Reverdin discovered that small, thin pieces of superficial skin, transplanted upon a healthy, granulating surface, formed, in a short time, organic connections with the granulations, and that epidermization proceeded independently from such transplanted islets of skin. Later, Schwenninger demonstrated, by his experiments, that hairs could similarly be transferred to a granulating surface. An open, granulating wound or ulcer can be covered over with epidermis in a short time by resorting to Reverdin's method of transplantation of skin. The most essential condition for success is an aseptic condition of the granulations. In suppurating wounds this method of treatment is not applicable until suppuration has ceased and the granulations are small and firm. The part from which the skin is to be taken, in preference the thigh or arm, should be shaved and disinfected. The only instruments required for cutting and transferring the skin is an ordinary sewing-needle fixed in a needle-holder, or, what is still better, a pair of hæmostatic forceps and a sharp razor. With the needle the skin is transfixed, and with a razor a thin section the size of the circumference of a split pea is removed and at once transferred to the granulating surface with the needle in such a manner that the cut surface is brought accurately in contact with the granulations. As the detached portion of skin always curls toward the raw surface at its margins, it must be carefully flattened out with the point of one or two needles, care being taken to imbed it well among the granulations without causing any bleeding. The grafts are planted in rows, commencing near the border and leaving small spaces between the separate grafts. Each row of grafts is then separately protected with a narrow strip of protective silk, and a thick, antiseptic compress is applied and retained by a bandage, which should exercise uniform gentle compression. The dressing should not be removed in less than a week. At this time the grafts will not only have become firmly attached to the subjacent surface, but each of them has become surrounded with a zone of new epithelial cells. As each graft now constitutes an independent centre of epithelial proliferation, the remaining portion of the granulation surface soon becomes paved by new epithelial cells, and epidermization and cicatrization are rapidly completed. The results obtained by this method of treatment have not always been such as to satisfy the earlier expectations. The new skin is but a poor substitute for the normal structure. Epidermization is hastened, and the results are better than after-healing without skin-grafting, but the ideal result, the formation of tissue resembling true skin, is not obtainable by this method of skin transplantation.

Skin-grafting in the Treatment of Recent Wounds.—If after an operation or injury it is found that a too extensive defect of the skin renders approximation by suturing impossible, the surgeon has it now in his power to supply the defect at once by taking large skin-grafts from another part of the body, or from another person, and planting them in the form of a mosaic upon the raw surface. This method of skin-grafting in the treatment of extensive superficial wounds, as after the extirpation of a lupus, or a surface epithelioma, was devised by Thiersch. Experience has shown that grafts of the whole thickness of the skin, and an inch square, if planted smoothly upon the raw surface and kept uninterruptedly in contact with the wound by an appropriate dressing, not only retain their vitality, but enter rapidly into organic connections with the part with which they have been brought into contact, and, at the same time, their anatomical and physiological properties are maintained to perfection. Thiersch found that after eighteen hours they were supplied with new blood-vessels, which could be successfully injected from the vessels of the part to which they had become adherent. This method of transplantation of skin is now extensively practiced in connection with plastic operations about the face. For such purposes the skin is taken from the region of the trochanters, as the skin here is almost or entirely devoid of hair. All bleeding from the wound to be covered with the grafts is carefully arrested by surface pressure before the grafts are planted, as it is necessary to secure accurate coaptation of the wound-surfaces in order to secure a favorable result. The modern method of performing rhinoplasty furnishes a good illustration of this method of skin transplantation.

As a matter of course, success by this method of skin transplantation can only be expected when the wound and grafts are aseptic, and the parts are kept in this condition at least until vascularization of the grafts has taken place. After the grafts have been planted the treatment of the wound is the same as in Reverdin's method. During the after-treatment it is important to secure rest for the part, and to prevent, by appropriate means of fixation, even the slightest displacement of the grafts in any direction. A good plan is to apply a thin plaster-of-Paris bandage over the dressing. Schede has substituted Thiersch's for Reverdin's method in the treatment of granulating surfaces by skin-grafting, and the results have been very gratifying. The granulating surface is transformed into a recent aseptic wound by removing the granulations with a sharp spoon. After all bleeding has ceased the wound is covered with large skin-grafts in the manner described. The skin obtained after this method of transplantation presents a normal appearance. I have repeatedly seen that, after excision of an epithelioma of the frontal or parietal region, a defect the size of the palm of the hand was healed

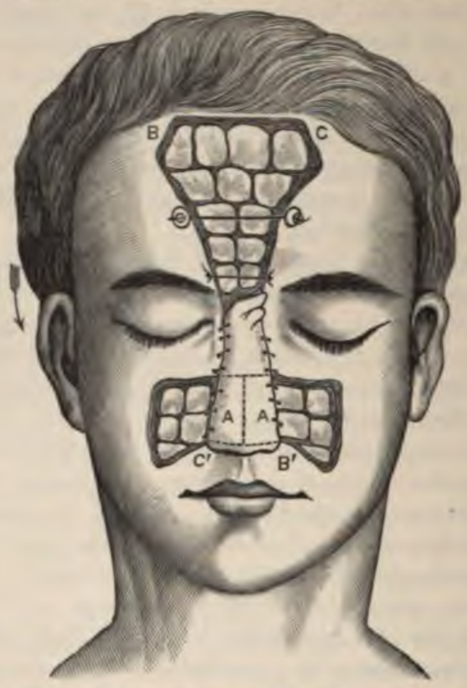

FIG. 20.—RHINOPLASTY AND TRANSPLANTATION OF LARGE SKIN-GRAFTS. (*Thiersch.*)

A, A, skin-flaps from face turned inward and covered with large flap from forehead, C after C′, and B after B′. Defects covered with mosaic of large skin-grafts from trochanteric region.

completely in less than three weeks by using Thiersch's grafts. This method of skin-grafting must be a welcome resource to the oculists in the operative removal of tuberculous lesions and malignant affections of the eyelids, as well as in the treatment of some forms of ectropion.

Transplantation of Mucous Membrane.—In the treatment of traumatic or ulcerative defects of accessible mucous membranes, it would seem that restoration of the defect by transplantation of grafts of mucous membrane, if found feasible, would be the ideal treatment. Wölfler has recently shown that such a method of treatment is not only practicable, but has resorted to it successfully in the treatment of obstinate strictures of the urethra. After excision of the cicatrix at the seat of resection he sutured a circular graft of mucous membrane to each end of the resected urethra, and had the satisfaction to observe that the graft not only retained its vitality, but became adherent and constituted an essential part of the new portion of the urethra. Wolfe has also succeeded in transplanting the whole of the tissues of the conjunctiva of the rabbit onto that of man in order to fill a defect caused by cicatricial contraction. This method of dealing with large defects of mucous surfaces accessible to direct treatment holds out many inducements for future imitation. The difficulties in the way of equal uniform success in the transplantation of grafts of mucous membrane, as in skin transplantation, are owing to the location of the seat of operation. In the former instance it must always be such as to preclude the possibility of securing perfect asepsis on the one hand, and the impossibility of applying an efficient protective dressing; at the same time, it is also more difficult to obtain the proper material for the grafting.

CONNECTIVE TISSUE.

The granulations seen upon a wound or ulcerating surface are formed almost exclusively by the transformation of mature connective tissue into embryonal tissue, the cellular elements of which they are composed being embryonal connective-tissue cells. This transition of mature into embryonal cells is accomplished by karyokinesis. As connective tissue is found almost in every part and organ of the body, it takes an active part in the repair of all wounds, and when the more important tissues in the wound cannot be approximated for organic union to take place its greater vegetative capacity enables it to produce a large amount of new material, which later forms a connecting bridge of cicatricial tissue. For instance, in a transverse wound of a muscle, where it is often difficult, if not impossible, to keep the divided ends sufficiently approximated for the wound to heal by the interposition of new muscle-cells, the gap is spanned by a band of connective tissue, which, if not completely, at least partially, restores the function of the muscle by furnishing it with two additional fixed points of attachment. Graser has shown that the first karyokinetic changes are seen in connective-tissue cells some distance from the surface of the wound, and that the new cells reach the surface with the new blood-vessels, where they constitute the granulation tissue. In aseptic wounds, where cicatrization progresses rapidly, the embryonal connective-tissue cells, or granulation cells, are short-lived, as they are rapidly transformed into mature connective tissue, which here constitutes the cicatrix. In suppurating wounds, the superficial layer of embryonal cells are brought in contact with the pus-microbes and their ptomaines, which destroy the protoplasm of the cells, when they are transformed into pus-corpuscles; while those nearer the blood-vessels retain their vitality and capacity of undergoing cicatrization.

BLOOD-VESSELS.

Wounds of large blood-vessels, with few exceptions, require such measures in their treatment which completely arrest the circulation, and which aim at permanent obliteration of the lumen by the usual method of cell proliferation and cicatrization. A wound of an artery, if accessible to direct treatment, should be treated by cutting the vessel completely across and applying a ligature to each end. A small wound of a large vein can be treated successfully, under favorable conditions, by closing it with a lateral ligature. With a tenaculum the margins of the wound are transfixed, and by making slight traction the vein-wall is raised, and around the base of the little cone thus formed a fine catgut ligature is applied. If the wound remains aseptic, the mural thrombosis at the seat of ligation is slight, and closure of the wound is effected without obliteration of the lumen of the vessel. A wound of a blood-vessel usually terminates, spontaneously or through the intervention of art, in permanent interruption of the circulation by the formation of an intra-vascular cicatrix. For many years it has been maintained that obliteration of a vessel after injury, disease, or ligature resulted from what was termed "organization of the thrombus." It was believed that the thrombus became vascular either from the lumen of the vessel or the vasa vasorum, and that the histological elements in the thrombus took an active part in the production of the intra-vascular cicatrix. Numerous experimental investigations by different authors, undertaken for the purpose of demonstrating that in wounds of blood-vessels healing takes place in the same manner as in the wounds of other tissues, have shown that the blood-clot always occupies only a passive rôle, and, if present, is only in the way of a speedy definitive closure, which invariably is effected by proliferation from the fixed cells of the vessel-wall. Eliminating the thrombus as an active agent in the obliterating process, we can say that union between the tissues which are brought in contact by the ligature takes place by tissue proliferation from the walls of the vessel itself. In the true sense of the word, direct or immediate union is as impossible here as in any other wound, and, like everywhere else, the intra-vascular cicatrix is formed from tissue derived from the tissue of the injured vessel-wall. In case the inner tunics are severed by the ligature, the lacerated surfaces are brought in contact with the adventitia, and repair takes place as in other tissues which are largely composed of connective tissue, the process extending from both sides of the ligature, where endothelia assist in the process of cicatrization. If, on the other hand, the continuity of the vessel is not destroyed by the ligature, and the intima is simply brought in contact without being ruptured, the new cells from the connective tissue perforate the endothelial lining, and the new elements of the latter join in the reparative process by being converted from their embryonal state into connective tissue. The histological changes in the interior of veins undergoing obliteration are the same as in arteries, the new material of which the cicatrix is composed being derived exclusively from the endothelial and connective-tissue cells.

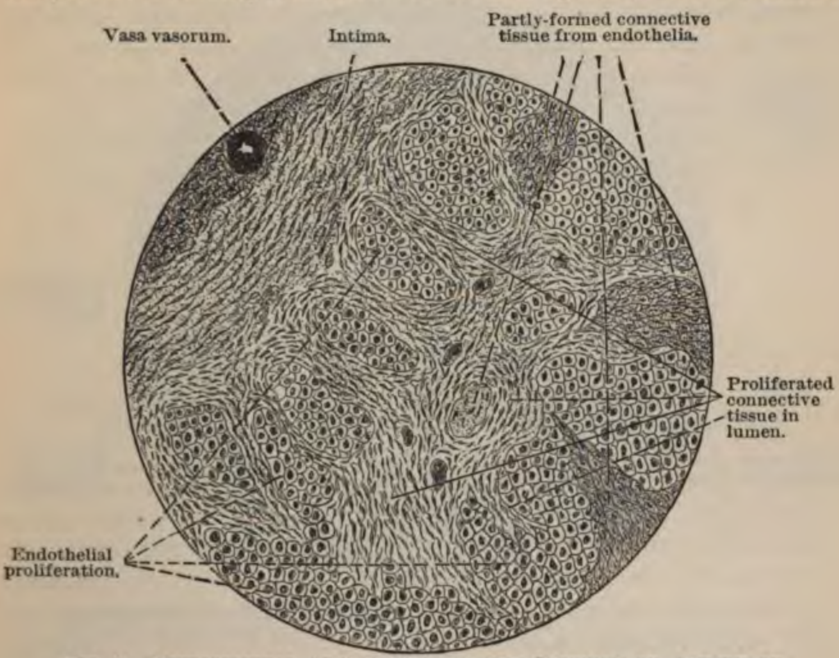
Vasa vasorum.
Intima.
Partly-formed connective tissue from endothelia.
Proliferated connective tissue in lumen.
Endothelial proliferation.

FIG. 21.—MICROSCOPICAL APPEARANCES OF THE INTERIOR OF ARTERY OF DOG FORTY-NINE DAYS AFTER LIGATION. TRANSVERSE SECTION THROUGH BORDER OF ARTERY. × 240.

J. Collins Warren, who has done excellent work in studying experimentally the healing of arteries after ligature, maintains that he has seen sufficient evidence in his specimens that the muscle-cells in the tunica media take an active part in the process of repair. The same author compares the process of healing in arteries to the formation of callus after fracture, and hence calls the intra-vascular material the internal and the extra-vascular the external callus. The numerous experiments of the author on ligation of arteries and veins have demonstrated, to his own satisfaction, that the most speedy obliteration of a vessel is obtained if the vessel is rendered bloodless by the application of two ligatures. The ligatures are applied with sufficient firmness to obliterate the lumen of the vessel *without rupturing any of its coats.* After ligation the walls of the vessel became thickened so that, a few weeks after the ligatures had been applied, the vessel presented a spindle shape, tapering toward each side, a condition entirely due to the formation of new material,—the external callus of Warren. The bloodless space between the ligatures is obliterated in a short time by cells which enter it from the vessel-wall.

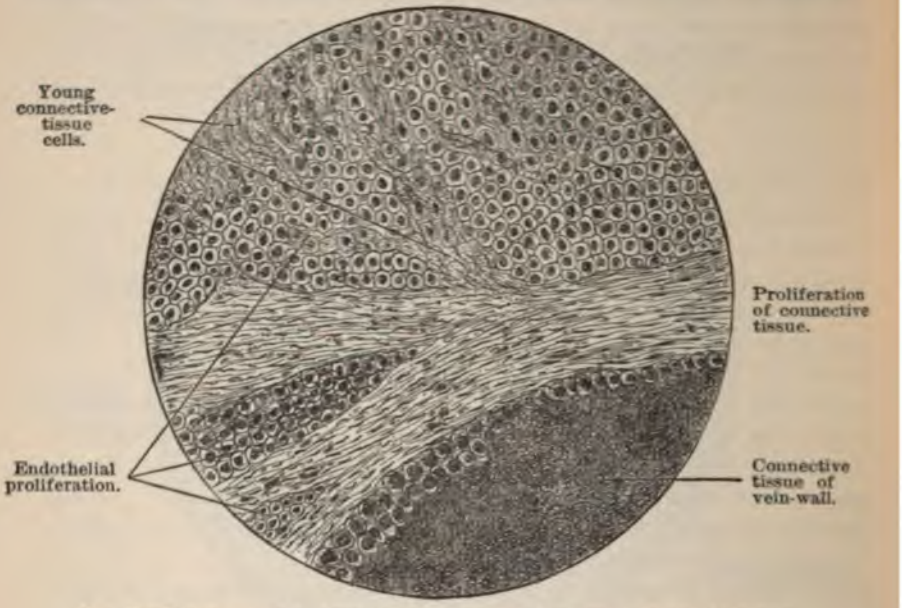
Young connective-tissue cells.
Proliferation of connective tissue.
Endothelial proliferation.
Connective tissue of vein-wall.

FIG. 22.—MICROSCOPICAL APPEARANCES OF THE INTERIOR OF VEIN OF DOG FORTY-NINE DAYS AFTER LIGATION. TRANSVERSE SECTION OF PART OF VEIN IN LIGATED PORTION. × 240.

In the obliteration of veins and ligation of arteries in their continuity, the double ligature, including a bloodless space about $\frac{1}{2}$ inch in length, places the tissues in the most favorable conditions for speedy definitive closure by an intra-vascular cicatrix. When the vessel is exposed catgut should be used, but in the subcutaneous ligation of veins silk is preferable. Since the introduction of antiseptic surgery and the aseptic ligature, secondary hæmorrhage has become an exceedingly rare accident, and, when it does occur, it is in wounds where the antiseptic measures have failed. A vessel in an aseptic wound, tied with an aseptic ligature, becomes in a few hours the seat of a regenerative process which effectually guards against the possibility of hæmorrhage, even if the mechanical obstruction caused by the ligature should be removed after a few days. The aseptic ligature, applied under strict antiseptic precautions, has been advantageous in other directions. The older surgeons always expected, after ligating an artery in its continuity, that the thrombus would extend on the proximal side to the nearest collateral branch, and on this account they were always anxious to secure a space of an inch or more between the ligature and the nearest large collateral branch, in order to prevent secondary hæmorrhage. The aseptic ligature is never followed by such extensive thrombosis, and the intra-vascular cicatrix is often exceedingly narrow,—in fact, almost linear. The limited thrombosis and the prompt formation of an intra-vascular cicatrix place the surgeon now in a position that he can ligate a large artery, close to a collateral branch or near a point of bifurcation, without a particle of fear of incurring secondary hæmorrhage. In the ligation of veins the aseptic ligature has dispersed all fear of suppurative thrombo-phlebitis and pyæmia,—complications which were formerly so much feared, even after insignificant operations on veins. In the repair of wounds union between the divided ends of blood-vessels is probably never effected. The vessel-ends are temporarily closed either by tying with a ligature or by the formation of a thrombus, the former being the case when vessels of some size have been divided, the latter being accomplished usually spontaneously in vessels which give rise to parenchymatous hæmorrhage. In either instance the ends of the vessel are, later, permanently sealed by the formation of a cicatrix by proliferation of fixed tissue-cells, the endo-

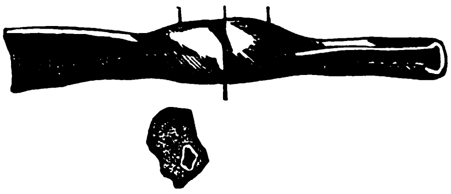

FIG. 23.—FEMORAL ARTERY OF DOG FIFTY DAYS AFTER DOUBLE LIGATION WITH SILK. BELOW, TRANSVERSE SECTION SHOWING BLOODLESS SPACE FILLED WITH CICATRICIAL MATERIAL. (NATURAL SIZE.)

thelia, and connective-tissue cells. The interrupted circulation between the two sides of the wound is restored indirectly through collateral branches, which are always new blood-vessels. The angioblasts in the injured capillary vessels assume active tissue proliferation within twenty-four hours after the injury has occurred, and through them, almost exclusively, the new blood-vessels are formed in the shape of loops, which, coming as they do from both sides, establish the vascular connection between the two surfaces of the wound. Many of these new blood-vessels disappear after the consummation of the reparative process, while others remain as permanent collateral vessels between the closed ends of the old blood-vessels permanently separated by the injury.

MUSCLES.

It is only quite recently that it has been ascertained that a divided muscle can unite, under favorable circumstances, by interposition of new muscular tissue between the divided ends. It was formerly believed that healing was always accomplished by the formation of connective tissue, and that the ends of the cut muscle remained permanently separated by a bridge of cicatricial tissue. The theory that connective tissue can be transformed into muscular tissue is untenable, since Pflueger has demonstrated the minute structure of muscular fibre. Kölliker has shown that the fibrillæ in the muscle-fibre constitute the real ground-substance. Rabl ascertained, by his embryological researches, that the muscular tissue is derived from a distinct portion of the mesoblast, and consequently proved that at a very early period of embryonal life an absolute difference takes place between muscular and connective tissue. Heterotopic muscular structures must, therefore, be looked upon, not as products of connective-tissue proliferation, but as a growth from a displaced embryonal matrix of muscular tissue.

The vegetative capacity of muscle-cells, striped and unstriped, is quite limited, as compared with some of the other tissues, so that if the ends of a muscle that has been cut transversely are separated for more than an inch complete restoration of the continuity of the muscle is not attaind, and the two ends are connected by a band of connective tissue. If, during the healing of the wound, the cut surfaces of the muscle are kept in accurate contact, and even if a gap of half an inch exist between them, restoration *ad integrum* takes place by proliferation of the muscle-elements near the seat of injury.

Non-striated Muscular Fibre.—Stilling and Pfitzner, as well as Busachi, have shown that unstriped muscular fibres multiply by indirect division of their nuclei, and in the repair of wounds of this tissue new fibres are produced exclusively by this method. These authors studied the karyokinetic changes in the muscular fibres of the *triton tæniatus*. They observed, after the division of the nucleus in the usual manner by karyokinesis, that as the new nuclei separated and approached the poles of the cell the protoplasm of the cell-body at the transverse axis became narrower, showing a well-marked constriction, which would indicate that subsequently cell-division occurred. Herczel witnessed similar changes in the hypertrophic muscular coat of the intestines on the proximal side of strictures. In defects caused by the injury, removal, or destruction of unstriped muscular fibres, regeneration takes place only from the margins, while the centre at first is occupied by connective tissue. The new muscular fibres are at first irregularly arranged, and it is only toward the completion of the healing process that the new tissue represents to perfection the mature muscular fibres. Klebs is of the opinion that the leucocytes serve as food for the cells which undergo karyokinetic changes.

Striated Muscular Fibre.—O. Weber, as early as 1854, claimed that in the healing of wounds new muscular fibres are produced, but, in accordance with the views which then prevailed, believed they were derived from connective tissue. Wittich saw, in hibernating frogs, new fibres which he believed had developed from the cells of the internal perimysium. In 1865, after an examination of a genuine myoma striocellulare, Buhl expressed the opinion that new muscular fibres are produced from old fibres. In the same year Waldeyer discovered the muscle-cell sheath, and he regarded the cell inclosed by it as a derivative of the nucleus of the fibre, but, with Zeuker and others, he still regarded the perimysium as the source of new muscular fibres. In 1868 E. Neumann made the observation that after section or laceration of a muscle the ends of the fibres became the seat of active tissue changes, which resulted in the formation of what he termed muscle-buds. These muscle-buds were not only found at the ends of the fibres, but also on their sides; at first they were seen to be composed of numerous nuclei and protoplasm, while later they were transformed into striated fibres. The sarcolemma is such a delicate structure that new cells which form within it readily find their way through it, and appear upon its outer surface in the shape of buds, as described by Neumann.

Tizzoni has recently investigated the karyokinetic changes in the nuclei or sarcoblasts in the perimysium during the repair of muscle wounds. The first evidences of cell proliferation were seen in the nuclei or myoblasts nearest the seat of injury, and proliferation took place in fibres which had undergone degeneration as well as in those which presented a striated appearance. Leven found, during the first twenty-four hours after injury, an increase of nuclei of the sarcolemma sheath. These new nuclei are arranged in the form of rows and heaps, and by mutual pressure are flattened. Many of these new elements present karyokinetic figures, and around them protoplasm is deposited, and the new cells become spindle-shaped. The new cells increase in number from the third to the fourth day, so that at this time from five to six can be seen under one field. Klebs studied regeneration of muscle in young guinea-pigs after puncturing subcutaneously the gastrocnemius muscle. He came to the following conclusions: A portion of the muscular fibres die and shrink, and in this condition they can be stained more deeply with hæmatoxylin than the others. Such fibres are completely removed by absorption within the first four days. In the fibres which remain striated the fibrillæ become plainer, and in them the regenerative process can be distinctly seen. The nuclei increase in number, and are packed densely together, but at this stage he was unable to detect any evidences of karyokinesis. During this stage Steudel was also unable to detect any appearances which indicated indirect cell division. These young cells are called sarcoblasts by Klebs, and their transformation into muscle-fibres is effected by aggregation around them of a very thin layer of protoplasm. The youngest cells are round, and the change into spindle form is gradual. The new cells are arranged in rows between the old muscular fibre (Fig. 24, between G and B). Some authors believe that the sarcoblasts unite end to end, and that the muscular fibre is formed in this

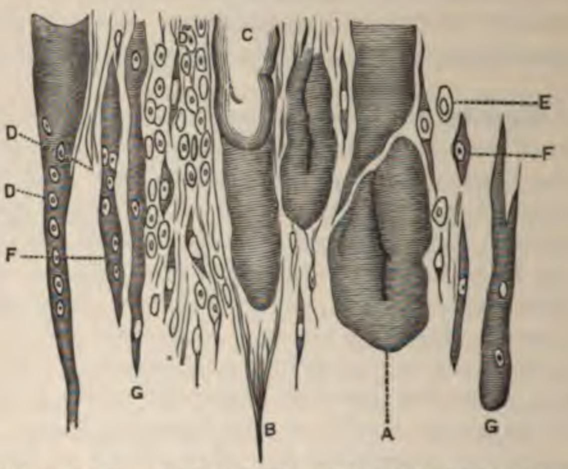

FIG. 24.—MUSCULAR FIBRES NEAR A WOUND IN A STATE OF PROLIFERATION. (*O. Weber*).

A, contused end of muscular fibre; B, muscular fibre retracted within sarcolemma, the latter terminating in a sharp point; C, old fibre degenerated into a colloid mass; D, young nuclei between and upon fibres; E, nuclei surrounded by cell-protoplasm; F, new cell, showing striations; G, new muscular fibre.

manner. Kraske and Klebs maintain that muscular fibres result from a single cell by gradual elongation of the cell-body. In the regeneration of the muscular fibres of the heart after injury, Martinti and Bonome witnessed karyomitotic changes in the interior of the sheath of numerous fibres, while in others where degenerative changes had taken place no such changes could be seen. In wounds of the heart of old rats karyomitosis commences five to six days after the injury, and does not last longer than six to seven days, and results only in incomplete regeneration. In myocarditis the formation of new muscular fibres has been observed by Virchow, Boettcher, and Waldeyer.

Muscle Suture.—In the treatment of recent wounds special pains should be taken to secure accurate approximation between the ends of divided muscles. For this purpose special means must be employed when large muscles have been divided transversely. In such cases the retraction which follows gives rise to great separation, which can only be overcome by suturing respective ends separately with buried animal sutures. Great care is necessary not to invert the margins, but to unite the cut surfaces throughout, using for this purpose, if necessary, as many as six sutures, which must include considerable tissue in order to prevent their tearing through. In muscles supplied with a well-marked sheath this should be sutured separately. In the after-treatment it is necessary to place the limb in such a position that will relax the sutured muscles, and to secure immobility of the limb in this position by a proper mechanical support, which should not be removed until the healing process is completed, in order to prevent subsequent diastasis between the sutured ends. When it is desirable to elongate a contracted muscle in the correction of deformities, as in the treatment of torticollis, the contracted muscle should be exposed by incision, and after section a *suture à distance* is applied. A number of heavy catgut sutures will answer an excellent purpose, as they will maintain fixation of the separated ends in a desirable position, and will furnish an admirable scaffolding for the new connective-tissue cells, which, later on, are transformed into a tendon which permanently connects the retracted ends of the divided muscle.

BONE.

The granulation material by which the fractured bone unites is called callus. According to the location of this material around, within, or between the fragments, we speak of an external, internal, or intermediate callus. The external or provisional callus is abundant, as a rule, where the broken bone is surrounded by a thick cushion of soft parts, and when the fragments are not well immobilized. It forms early and disappears gradually after the fracture has united. The internal or medullary callus, which takes the place of the medullary tissue in fractures of the shaft of the long bones, serves a useful purpose as a means of fixation of the fragments, and is also removed in the course of time after union has taken place, and with its disappearance the medullary cavity is restored. The intermediate or definitive callus is the material interposed between the broken surfaces, and which is transformed into permanent tissue. Callus is the product of cell proliferation of those tissue-elements which are directly concerned in the growth and development of bone.

Duhamel de Monceau attributed to the periosteum and endosteum the function of producing callus. Haller and his prosector, Detlef, believed that the periosteum takes no part in the regeneration of bone, but that callus is derived from the fractured ends of the bone, more especially the myeloid tissue. Dupuytren maintained that the periosteum and the paraperiosteal connective tissue were bone-producing tissues. Cruveilhier claimed that the lacerated soft tissues around the fractured bone-ends, the periosteum, connective tissue, muscles, tendons, etc., furnished the material for the callus.

Flourens claimed that the periosteum alone could produce new bone. Rokitansky asserted that callus is developed directly from bone and its connective tissue, including the periosteum. From his own experimental work, R. Hein came to the conclusion that regeneration of bone takes place from connective tissue in and around bone and the periosteum. According to Virchow, callus is produced from connective tissue outside of the bone, as well as from the medullary tissue. Hofmokl considered as sources of callus formation the periosteum, bone, and marrow. Gegenbauer takes the ground that bone is produced directly from connective tissue. He asserts that Sharpey's fibres, if traced carefully, can be seen springing from a bony point between the Haversian canals, from which point they radiate toward both sides into the lamellar systems. The fibres form net-works, and at points of intersection bone-cells are produced, and a deposit of lamellæ takes place around the connective-tissue fibres.

It is now generally conceded that the provisional callus is the product of tissue proliferation from the periosteum, while the definitive or permanent callus is produced directly from the medullary tissue. The provisional callus is nature's splint, its only object being to immobilize the parts until the definitive callus firmly and permanently unites the fragments. The temporary callus is an accidental product, and appears earliest and most copiously where the paraperiosteal tissues are most abundant and motion between the fragments greatest; the intermediate or permanent callus is produced later, and is transformed into permanent tissue. Ollier and Buchholtz, in their experiments on transplantation of periosteum, found that the transplanted tissue first produced cartilage, which later was transformed into bone; but they also ascertained that such bone disappeared again unless it formed in a place where bone normally exists. Cohnheim and Maas came to the same conclusion from their experiments on intra-venous transplantation of periosteal grafts. It is possible that special cells (Mastzellen) are the active agents in the removal of tissue in places where it has no physiological existence.

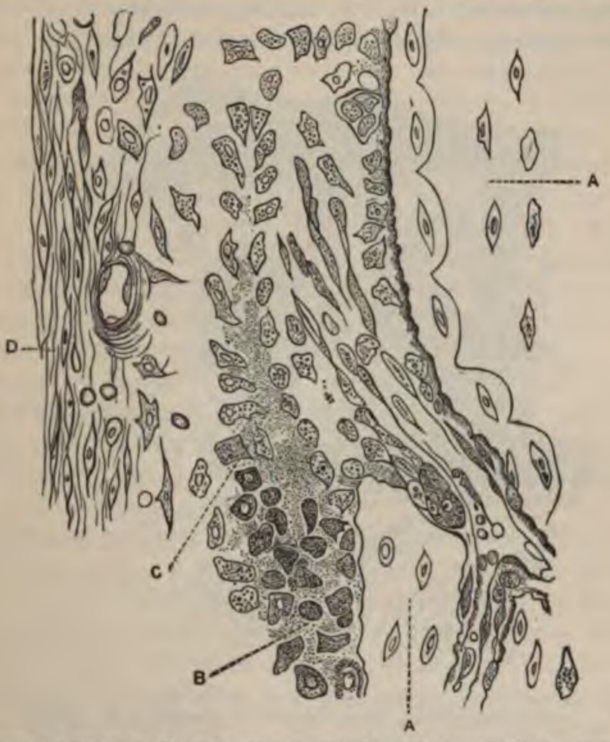

FIG. 25.—SECTION THROUGH CALLUS FIFTY-TWO HOURS AFTER FRACTURE OF ULNA FROM RABBIT. BEGINNING FORMATION OF OSTEOID TISSUE. (*Bajardi.*)

A, cortical portion of bone; B, osteoid tissue; C, beginning of formation of a lamella, surrounded by osteoblasts; D, periosteum. (Hartnack, Obj. 8.)

Macewen has maintained for years that bone grows only from bone, and the results obtained by applying this principle in practice speaks strongly in favor of this supposition. That medullary tissue alone can produce bone has been experimentally demonstrated by Burns. The osteoblasts from which bone production alone can take place are found in the periosteum, more especially its inner layer, the cambium, and in the interior of bone. Regeneration of bone from these cells takes place in two ways,—either the cells are transformed into an osteoid tissue, or they are first changed into cartilage-cells, and the latter at a later stage undergo ossification. The osteoblasts in the periosteum, and, to a lesser extent, those in the central medullary cavity, produce bone by this indirect method, while in other places ossification is effected in a more direct way by the osteoblasts being transformed into an osteoid substance.

In the normal regeneration of bone, cartilage plays an important part. As the bone-cells disappear, or at least lose their nuclei where cartilage-cells form, it is probable that the cartilage-cells represent structures intermediate between osteoblasts and bone-cells. Cartilage is abundant where union is retarded, and especially in cases of pseudarthrosis. During ossification the hyaline cement-substance between the cartilage-cells is dissolved, and the space gives way to lamellæ, while the cells are transformed into bone-cells. According to Krafft, multiplication of the bone-producing cells of the periosteum can be seen twenty to thirty hours after fracture, in the shape of karyokinetic figures in the nuclei of the cells, while somewhat later the same figures are to be seen in the endothelia lining the blood-vessels. The new cartilage-cells also multiply by karyokinesis. Like in the healing of wounds in soft parts, the cells on the surface of the fracture take no part in the process of

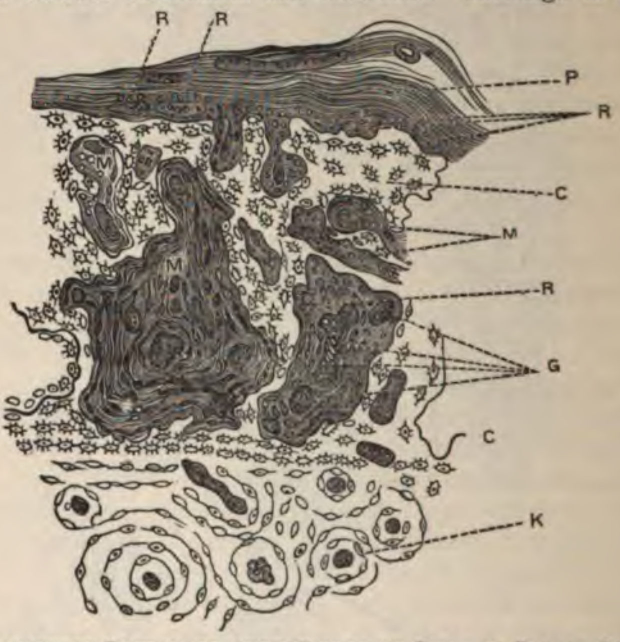

FIG. 26.—TRANSVERSE SECTION THROUGH CALLUS OF TIBIA OF RABBIT FORTY DAYS AFTER FRACTURE, WITH EXTERNAL RESORPTION. (*Maas.*)

P, periosteum, much thickened; R, giant cells or osteoklasts; G, blood-vessels; M, medullary resorption spaces; K, compact portion of bone.

regeneration, as their proliferation capacity has been destroyed by the trauma as well as the sudden diminution of the vascular supply. Osteoporosis at the seat of regeneration is always present, and results from the action of another kind of cells discovered by Kölliker,—the osteoklasts. Robin described them as myeloplaques. They are found in Howship's lacunæ where resorption takes place.

The osteoklasts appear to be nothing else but myeloid cells which have lost their bone-producing function; they are in reality hyperplastic osteoblasts. Absorption of bone takes place because these cells do not produce bone. There is no reason to believe that these cells are altered bone-cells, as no intermediate forms have been found. Ziegler does not assign much influence to these cells in the resorption of bone. Wegner has shown that in pathological processes in bone where resorption takes place they are arranged along the sides of blood-vessels, and on this account he believed they were derived from the vessel-wall. Klebs is of the opinion that the osteoklasts may secrete a chemical substance which decalcifies the bone. Resorption of superfluous callus is accomplished undoubtedly by the action of osteoklasts, an exceedingly useful function, as by it form and strength of the broken bone are restored.

According to Meyer the architectural structure of the spongiosa, after the healing of a fracture, adapts itself to the new conditions, so that the new traction and pressure-curves are arranged in such a manner as will resist the greatest degree of force. This capacity of adaptation is present to a very high degree in bone.

Abnormal and Defective Callus.—Callus may be formed in excess of local requirements after a fracture, and yet no union take place. The osteoblasts respond promptly to the stimulus created by the trauma, karyokinetic changes occur early, new cells are formed with great rapidity, and a large mass of new material is deposited at the seat of fracture, but bony consolidation does not occur because the new tissue does not undergo ossification. The normal development of cells is arrested at an early stage, and the chemical process upon which ossification depends are delayed or fail to appear altogether. Prompt bony union does not only imply that the osteoblasts at the seat of fracture should undergo karyokinetic changes and multiply, but that the new tissue must be placed under the influence of favorable chemical conditions which will enable it to be transformed into bone.

A few years ago B. von Langenbeck reported 2 cases of fracture of the femur, where he resorted to amputation of the thigh under the belief that the luxuriant callus, which formed in each case at the seat of fracture, was a sarcoma. Microscopical· examination in both instances showed that the swelling was composed of cells which are found in callus at an early stage of its formation, without any evidences of ossification of the new material. The causes of delayed ossification are not known, but, as in a number of instances of profuse callus formation and delayed union a vigorous antisyphilitic course of treatment produced favorable results, it appears that the virus of syphilis may at least be one of them. We know that in gummata the same conditions prevail in the persistence of tissue in its embryonal state for an indefinite period of time, or until the syphilitic virus has been removed or neutralized by proper antisyphilitic treatment.

In cases where no such cause for the delay of the transition of callus into bone can be surmised, the internal administration of minute doses of phosphorus should be tried. Kassowitz produced osteoporosis in animals experimentally by large doses of phosphorus, while minute doses produced an opposite effect. He recommended the remedy in small doses in the treatment of rickets, and since then it has been extensively used in the treatment of this disease, and with the best results. The action of this drug undoubtedly would produce a favorable effect upon the osteoid material, in hastening its transition from the embryonal into a mature state. Defective callus formation will necessarily follow a fracture if the osteoblasts fail to enter upon an active process of cell proliferation. These are the cases where the surgeon resorts to local measures, which are intended to stimulate the cells to increased activity. Fractures of the lower extremities which have failed to unite as long as the patient is kept in bed often unite promptly after he is allowed to walk around on crutches, the favorable change being brought about by an increased blood-supply to the seat of fracture.

Dumreicher suggested that the local blood-supply could be increased by applying a compress and bandage above and below the seat of fracture, while Helferich more recently, and with the same object in view, advised moderate constriction with an elastic bandage applied in such a manner as not to interfere with the arterial circulation. Rubbing of the fragments forcibly against each other is an old method of treating delayed union, and has often been sufficient to rouse the dormant osteoblasts into active cell proliferation. The distinguished Brainard made the treatment of delayed union a special study during many years of his useful life, and devised a new method of treatment, the subcutaneous drilling of the ends of the fragments, which has been extensively practiced, and has yielded most excellent results. The drilling of the ends of the broken bone has a most decided effect in stimulating the sluggish separative process, as it produces osteoporosis and increases the vascularity of the parts, both of these conditions being well calculated to increase the local nutrition. Dieffenbach went one step farther, and advised the use of ivory nails, which were allowed to remain until they became loose and dropped out. The term *non-union* is a relative one, as in some fractures this condition may have been reached in three to four months, while others may unite after a year.

In a fracture of the femur in a healthy man, who came under the author's observation, that had not united a year after the accident, bony consolidation took place after this time without any operative interference. In another case bony union did not occur until nearly two years after the fracture had taken place. When a pseudarthrosis has once become established, all measures which have been found useful in the treatment of delayed union are useless, and the only rational treatment in such cases consists in transforming the old fracture into a recent one. The ends of the fragments are exposed, the interposed ligamentous structures—muscles or tendons—or false joint excised, and the ends vivified in such a manner as to furnish large surfaces for apposition. The bone should never be cut transversely, but always obliquely, or, what is still better, Volkmann's step-operation should be done wherever the existing conditions make this possible. Direct fixation of the fragments with aseptic bone or ivory nails should always be practiced, as by this expedient we are able to secure greater immobility between the fragments, and at the same time the perforations and the presence of the foreign bodies cannot fail in imparting an additional stimulus to the tissues which will expedite the process of repair.

The frequency with which non-union is met with after intra-capsular fracture of the neck of the femur has almost by universal consent been attributed to defective callus formation. It has been claimed that in such a fracture, occurring as it usually does in persons advanced in life, callus production is always defective, and, as the upper fragment is but scantily supplied with blood-vessels, it was asserted that it was not in a condition to take an active part in the reparative process. The author made numerous experiments on animals, fracturing the neck of the femur within the limits of the capsular ligament, and as long as the fracture was treated in the customary way bony union was never attained. He then resorted to direct means of fixation by transfixing both fragments with an absorbable nail, and with this treatment succeeded in obtaining bony union in the majority of cases. Since that time he has treated fractures of the neck of the femur by immediate reduction and permanent fixation with a plaster-of-Paris splint, with pressure over the trochanter major in the direction of the axis of the neck of the femur with a compress and set-screw, the latter passing through a splint which is incorporated in the plaster-of-Paris dressing. With this treatment he has obtained bony union in a number of instances, where all the signs and symptoms pointed to a fracture within the capsular ligament.

It is a well-established clinical fact that in the aged other fractures unite readily, and pseudarthrosis is exceedingly uncommon, excepting after this fracture; and the writer is satisfied that this undesirable result occurs more in consequence of improper treatment than defective callus production. If the fragments can be brought in accurate apposition soon after the accident has occurred, and coaptation can be maintained uninterruptedly for three months by an appropriate dressing, bony union can be secured not only in exceptional, but in the majority of, cases. In the treatment of fractures, as in the treatment of wounds of the soft parts, accurate coaptation and effective fixation should be aimed at so as to place the parts in the most favorable conditions to unite by the smallest possible amount of new material.

GLANDS.

Griffini studied regeneration of testicle-substance in frogs, dogs, chickens, and guinea-pigs. He excised a wedge-shaped piece under strict antiseptic precautions, and killed the animals in from three to seventy-five days. Examination of the specimens showed that an increase of tubuli seminiferi had invariably taken place. They appeared to have originated as blind pouches from pre-existing tubules. Tizzoni has also observed, in his experiments on dogs, production of new gland-tissue during the healing of wounds of the liver and after partial excision of this organ. The same author studied experimentally regeneration of the spleen-tissue, and found that this occurred after partial and complete extirpation, the new tissue being made up of elements in connection with blood-vessels of the adjacent peritoneum. After complete extirpation of the organ the new spleens appear as nodules of a brownish color, which are attached to the vessels of the peritoneum, and develop around new buds of these vessels. The beginning of such a minute spleen appears as an accumulation of new loose connective tissue, in the meshes of which lymph-corpuscles are found; later, follicles and pulp-substance appear, with a corresponding arrangement of blood-vessels. As these little organs always appear about the hilus of the spleen, they cannot be supernumerary spleens. After excision of wedge-shaped pieces of the spleen, formation of new spleen-tissue has also been observed upon the omentum at a point opposite the wound and independently from tissue proliferation in the wound. Reproduction of tissue therefore takes place in the same manner as in the regeneration of lymphatic tissue. After the removal of the entire spleen, tissue proliferation takes place in the adjacent blood-vessels, the product of which corresponds with normal splenic tissue, and doubtless possesses the same physiological functions. As the immediate result of such proliferation an altered condition of the vessels must be accepted, as the blood-vessels of the omentum and peritoneum correspond with the fundus of the stomach. Mayer claimed regenerative capacity for the pulp of the spleen, but he may have been deceived by the presence of lymphatic glands of the color of the spleen at the seat of extirpation. Picard and Malassez, Bizzozero and Salvioli, and finally Tizzoni and Fileti showed that after splenectomy a diminution of the blood-corpuscles is observed first, but as the new spleen-tissue is produced their number again increases. Baier and Bacialli have shown, by their experimental investigations, that new lymphatic tissue is rapidly produced after partial as well as after complete removal of a lymphatic gland. In the regeneration of this tissue the adjacent adipose tissue appeared to take an active part. According to Baier, the adipose tissue is first infiltrated with leucocytes, while Bacialli saw new endothelial cells and lymph-spaces develop from the connective-tissue cells, after having seen mitotic figures in the nuclei. After complete extirpation of a lymphatic gland, reproduction of lymphoid structure in all probability does not take place from any other but lymphatic tissue, and the new gland-tissue is the product of tissue proliferation from the cut ends of lymphatic vessels.

CENTRAL NERVOUS SYSTEM.

The central nervous system is built up partly from the mesoblast and partly from the epiblast. The stellate and spider-shaped cells are derived from the mesoblast, while the neuroglia and the nerve-cells proper spring from the neuroblast, a part of the epiblast, which, in the embryo, is located nearest the middle axis. The neuroglia represent channels of nutrition, which are formed only at a time when the neuroblastic tissues have reached the height of their development. The mesoblastic portion of the brain and spinal cord does not increase during the healing of a wound of these parts. In pathological conditions, however, as in cases of multiple sclerosis, the stellate and spider-shaped elements proliferate so actively that the nerve-cells are completely displaced by the new product. Many authors have expressed their doubts as to the possibility of regeneration of brain-tissue after injury or disease, while others have gone to the opposite extreme, and claim that complete repair can take place in cases of extensive defects. Voit claims that in pigeons he has observed complete restoration of both structure and function after extirpation of the entire cerebrum. While large defects are not repaired, the regenerative capacity of the nervous elements cannot be doubted, and such a doubt would come in conflict with a general law. Regeneration of the cerebral nervous system comprises the production of new ganglia-cells and neuroglia, the latter consisting of a fine net-work, sometimes of nervous, at others of basis, substance. During the healing of every wound of the brain the observer can satisfy himself that the neuroglia possesses a high capacity of reproduction, as well-marked karyokinetic changes can be seen during the first twenty-four hours after the injury. The new cells are very abundant, and arrange themselves in groups. More difficult is the demonstration of the same changes in the ganglia-cells, but Mondino (1886) and Coen (1887) have given descriptions of these cells which leave no further doubt that they also multiply by karyokinesis. Klebs has also observed karyokinetic figures in the nuclei of ganglia-cells during the repair of injuries of the brain. In the embryo, increase of ganglia-cells by karyokinesis has been witnessed by Pfitzner, Uskoff, Rauber, Merk, and Cattani. It is true that brain wounds heal with some defects, but this applies to extensive injuries in which the regenerative capacity of the brain-substance is not equal to the emergency; hence, only a part of the defect is repaired. Klebs gives an accurate account of his examination on the reparative process in two cases of brain injury,—one recent, the other of long standing. Microscopical examination of the tissues from the seat of injury in both cases showed that new tissue had been produced. He found many new cells from the neuroglia which he is inclined to believe may functionally take the place of ganglia-cells. The same author made numerous experiments on young animals for the purpose of studying the process of healing in wounds of the brain. With an aseptic needle the brain was punctured. No symptoms followed the injury. The brain was examined from two to four days after puncture; only slight meningeal hæmorrhage. The needle-track in the brain not closed. Mitotic changes were found not in the cells in the immediate neighborhood of the puncture, but in the cells corresponding to from the second to the fifth row from it. In the same place were found an accumulation of resting nuclei. Mitotic cell proliferation of injured cells was found completed on the fourth day. Ganglia-cells undoubtedly increase in number in the same manner. He found no leucocytes in the brain, and believes that those that must have been present had been appropriated as food by the cells which had undergone karyokinetic changes. The gray matter of the surface of the brain is composed of numerous but exceedingly small cells, and their numerous connections would indicate great reproductive capacity.

Peripheral Nerves.—When Cruikshank suggested the possibility of restoring physiological function in a divided nerve by suturing, his contemporaries regarded the suggestion as an absurdity. Since that time the subject of nerve regeneration has engaged the attention of some of the best men in the profession, and from the knowledge which has thus accumulated it is safe to repeat the statement made by Vanlair recently, that "the surgeon who neglects to suture a divided nerve commits the same mistake as he who neglects to reduce a fracture or fails to unite a divided tendon." Regeneration of a nerve takes place exclusively from pre-existing nerve-fibres. Schwann's sheath isolates the nerve-fibre so thoroughly from the mesoblast that it would be almost impossible for the latter to take any direct or active part in the regeneration of the former. The neuroblasts from which tissue proliferation takes place are found within the nerve-sheath. Confluence of the new nerve-elements within the neurolemma does not take place, as, according to Cattani, they receive envelopes from the medulla. Section of a motor fibre is at once followed by degeneration of the motor terminal palate; hence, degeneration and regeneration in the divided nerve and the muscles supplied by it are parallel processes. Degeneration and regeneration have been studied in nerves that were stretched, lacerated, or completely cut across, and the histological processes were found almost identical in all of these conditions. The study of degenerative and regenerative processes side by side in injured nerves has thrown much light upon their minute anatomy. The medullated peripheral nerve-fibre is composed essentially of Schwann's sheath, the axis-cylinder, and a fluid which appears as a periaxial layer. Klebs looks upon this fluid as a sort of nervous endolymph, which, by virtue of its great mobility, takes part in the nutrition of the nerve. The space which contains the fluid, being between the axis-cylinder and the sheath, serves not only the purpose of a channel for the fluid, but also for the dissemination of movable elements, as, for instance, migration corpuscles. Leucocytes are only present in any considerable number in pathological conditions. Schwann's sheath is composed of connective tissue. The large oval nuclei, containing each one or two shining nucleoli, which are attached to its inner side, are the neuroblasts. It is as yet not definitely settled whether the portion of nerve between two of Ranvier's constrictions is composed of one or more cells. Klebs is inclined to accept the view that such a space is represented by one cell, and if several nuclei are present they are the product of nuclear segmentation. The nuclei must be regarded in the light of peripheral nerve-cells. The specific functional contents of a nerve-fibre are the axis-cylinder, the endolymph, and medulla. The first two are continuous with the neighboring elements, but not so the medullary sheath. The medullary sheath is a very complicated structure. The masses of fat are held together, and are inclosed by a frame-work of keratin. Finer keratín threads unite both sheaths in the form of Golgi's spirals, which are present in the funnels of Schmidt-Lautermann's medullary spaces; besides, numerous transverse threads are strung out in zigzag shape between the sheaths. The constituent parts of the medullary portion of the nerve-fibre can disappear separately; if the medullary fat is removed by absorption, the keratin frame-work becomes visible,—a condition which is present during the early stages of neuritis parenchymatosa; if the keratin frame-work is dissolved, the fat appears in drops, as can be seen during the degeneration of a nerve after section. The axis-cylinder is a pre-existing structure, which, however, can be only distinctly outlined against the medullary sheath and endolymph by post-mortem influences. Its structure, in the larger medullated fibres at least, is not simple, but is composed of fine fibrillæ, held together by an amorphous, gelatinous substance. Physiologically, this part of the nerve must be regarded as a complex of different conductors, which only differ by the qualities of motility and sensibility. Regeneration of a peripheral nerve-fibre is a regular typical process, as far as it serves as a substitute for lost elements of a nerve. The process resembles the physiological growth of a nerve which always occurs only in connection with the central nervous system. If the separation between the nerve-ends exceeds an inch, restoration of its continuity without assistance cannot take place. In such an event the ends become bulbous, the medullary substance in the distal portion undergoes degeneration, and the axis-cylinder becomes more and more indistinct. The same changes take place in the nerve-ends after amputation. When a nerve is simply divided, and there is no loss of substance, the ends remaining in close contact, function is established in a remarkably short time. In two instances Gluck observed perfect function within twenty-four hours. He concludes that the granulation tissue must have been the means of conduction in these cases. In his experiments on the sciatic nerve in fowls, where he divided the nerve and immediately sutured with catgut, function was restored in from fifty to eighty-six hours. Waller and Vanlair are of the opinion that regeneration proceeds entirely from the proximal end. Colasanti claims that degeneration of the peripheral end only extends as far as the next Ranvier's ring, while Tizzoni found that degeneration extends from the seat of injury in both directions, only that it is more marked on the distal side. Most of the recent writers on the subject assert that when a piece of the nerve is resected the entire nerve on the distal side undergoes degeneration, while, if the nerve is only divided, and the ends are immediately sutured, at least a number of the nerve-fibres retain their integrity. Eichhorst and others, who have made regeneration of the nerves a special study, are of the opinion that the nerve-fibres of both ends participate in the process of repair, and that regeneration commences with degeneration. Eichhorst believes that regeneration takes place exclusively by splitting of the axis-cylinder within Schwann's sheath, so that the latter in the course of time becomes distended with them. Continuity is restored by the central fibrils being pushed outward through the cicatrix to meet the peripheral, and coalescence follows. Beneke, on the other hand, traced the origin of the new fibres to protoplasm of the neuroblasts, which are transformed into delicate fibrils, which become surrounded by a coating of myeline, the future medulla. It is more probable that regeneration of a nerve takes place by the latter method. After a trauma, reproduction of the axis-cylinder always follows. According to a number of investigators who have studied this subject, several axis-cylinders are formed within each Schwann's sheath, each of which is surrounded by a separate medullary sheath. It is difficult to ascertain whether these new fibres, growing out of one of the old fibres, again become united some distance toward the periphery, or whether they remain isolated to their point of peripheral distribution. After nerve section, the axis-cylinder swells at the cut end and becomes striated; this swelling, however, is not an active process, but the result of imbibition of stagnant endolymph. The longitudinal striations and formation of vacuoles which have been described by Tizzoni are due to the same cause. The granular appearance is brought about by disintegration of the fibrillæ. The old axis-cylinder breaks down into isolated fragments, which, in part at least, are removed by leucocytes, which at this time have made their appearance. With such extensive destructive changes in the axis-cylinder it is difficult to conceive how regeneration of this structure could take place in the manner described by Eichhorst. The only histological elements within the fibre-sheath exempt from degeneration are the nuclei of the inner surface of the sheath, the neuroblasts, and from these regeneration takes place.

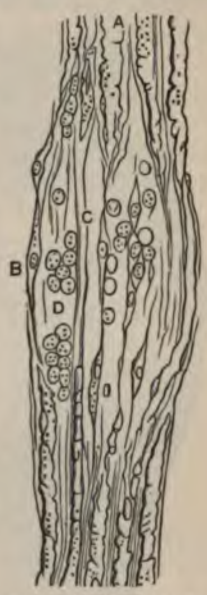

FIG. 27.—NERVE-FIBRE IN A STATE OF REGENERATION FIFTY TO SEVENTY HOURS AFTER INJURY. (*Gluck.*)

A, proliferation of neuroblasts; B, spindle-cell, which, becoming confluent with similar cells from both sides, unites the nerve-fibres; C, rows of spindle-cells, forming amyelinic nerve-fibres; D, young amyeloid cells, formed from nuclei of neurolemma.

At the seat of regeneration the nerve is enlarged from the accumulation of the products of tissue proliferation within the neurolemma sheaths.

The first stage of regeneration of a nerve is initiated by multiplication of the neuroblasts and increase of protoplasm. The nuclei increase to double their normal size and then divide into two or more. Division of nuclei probably takes place by karyokinesis. The protoplasm is granular, and is stained a reddish color with neutral picrocarmine. The nerve-fibre originates from the protoplasm, and, according to Tizzoni, in the form of separate pieces, around which already can be distinguished a medullary sheath and transparent contents. In other cases there may be a direct connection between the old and new axis-cylinder. Longitudinal striation of the axis-cylinder probably takes place at a time when the fibre has formed a direct connection with distant parts, the seat of active physiological processes. Leucocytes have been found within the neurolemma by Tizzoni and Korybut-Daskiewicz, while Neumann denies their presence in this locality. Cattani believes that they are present within the fibre-sheath after nerve-stretching, and can be found as far as the motor ganglia of the cord. Nerves of different function, when united, will undergo repair and establish useful conductors for the transmission of nerve force. The late Professor Gunn established the correctness of this assertion by a series of interesting experiments on dogs. Early functional results after nerve suture are often fallacious, as the function attributed to sutured nerves may be performed by other nerves which reach over such areas; and, again, the peripheral manifestation may be the result of physical conduction of the irritation, and apparent motor recoveries may be stimulated by the action of muscles other than those supplied by the sutured nerve.

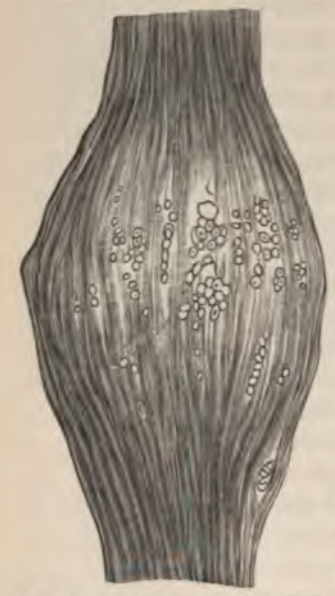

FIG. 28.—LONGITUDINAL SECTION THROUGH NERVE TWENTY-ONE DAYS AFTER INJURY, SHOWING MEDULLATED AND NON-MEDULLATED NERVE-FIBRES WITH ROUND CELLS BETWEEN THEM. (*Gluck.*)

NERVE SUTURE.

Nerve suture was first performed by Baudens in 1836, with negative result. The procedure was revived by Nélaton in 1863, and the following year by Langier. The first operations were made with fine silk sutures, which were not cut short, and subsequently came away by suppuration. O. Weber advised to unite the nerve-ends by passing the sutures, not through the nerve-substance, but only through the connective tissue surrounding the nerve,—the paraneurotic suture. Experience, however, has shown that transfixion of the nerve-ends by the sutures does not give rise to pain, and does not interfere with the normal reparative processes, and at the same time, by resorting to this direct method of suturing, more perfect coaptation is secured. In the case of large nerves, it is advisable to re-inforce the direct sutures with a number of paraneurotic sutures. The best material for the sutures is aseptic catgut. An ordinary sewing-needle with a dull point is preferable to a surgical needle, as it is more sure to pass through the nerve without injuring the fibres.

From one to three direct sutures, according to the size of the nerve, are applied, and from three to six paraneurotic sutures. The needle is passed straight through the nerve on each side, one-eighth to one-fourth of an inch from the ends, and care must be exercised, in tying the sutures, to bring the cut surfaces in accurate apposition, and not to tie the sutures too tightly, as by doing so the nerve-ends are liable to become displaced by overlapping. In tying the paraneurotic sutures the necessary precautions must be taken to prevent the margins of the sheath from insinuating themselves between the nerve-ends.

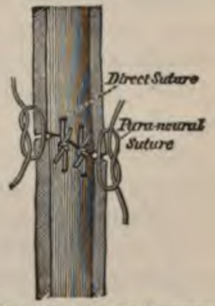

FIG. 29.—NERVE SUTURE, SHOWING APPLICATION OF DIRECT AND PARANEUROTIC SUTURES.

Primary Nerve Suture.—A primary nerve suture is one used to unite a nerve immediately or soon after the injury has occurred, and before any degenerative changes have taken place. It should always be resorted to in the treatment of accidental wounds where one or more nerves have been divided, also where in operations a nerve has been divided accidentally, and, finally, in cases where a neurectomy for pathological conditions cannot be avoided. The results after primary suture have been very satisfactory. Bruns has collected 71 cases from different sources, and in more than 33 per cent. of the number function was restored. As suppuration in a wound where a nerve has been sutured would, in all probability, cause tearing out of the sutures and displacement of the nerve-ends, it is of the greatest practical importance to secure for such wounds an aseptic condition and to obtain primary union throughout, and consequently no provision for drainage should be made. If the wound-surfaces cannot be approximated, and a greater or less space has to fill up by granulation, a bundle of catgut threads can be used for a capillary drain, in order to avoid tension from the accumulation of blood or the primary wound-secretion.

Secondary Nerve Suture.—When a divided nerve fails to unite, the ends become bulbous, are usually found imbedded in a mass of cicatricial tissue, and separated from each other from 1 to 2 or more inches. Function below the point of division is completely lost; the distal portion of the nerve itself, being no longer in connection with the central nervous system, undergoes degeneration, and the muscles supplied by the injured nerve become atrophic and useless. The reuniting of such a nerve is done by the secondary suture. Experience has shown that function can be restored by this procedure years after the injury. Jessop vivified the nerve-ends and applied sutures nine years after injury of the median nerve, and restored function. Langenbeck sutured the sciatic nerve two years after division; sensation returned in three days, and, later, motion. As a rule, sensibility returns first after nerve suture, followed considerably later by restoration of motor function. The most speedy restoration of function, both sensory and motor, after secondary suture is reported by Tillaux. He operated on the median nerve three years after division. The ends were found imbedded in a cicatrix and separated from each other 4 centimetres. The ends were vivified and sutured. He claimed that physiological function was restored completely three hours after the operation. There can be no doubt of the ultimate recovery of nerve function in this case, but that this should have been attained in three hours appears next to impossible. Enough has been said to show that secondary nerve suture can be resorted to with good prospects of success years after an injury, but for well-known reasons it should not be postponed after it has become evident that union has failed to take place. Unnecessary delay is dangerous, because when a nerve has become permanently disconnected from the central nervous system muscular degeneration goes hand in hand with degeneration of the distal portion of the nerve, and the longer the operation is delayed the greater the length of time required to complete the regeneration of the nerve and the muscles. The first secondary nerve suture was made by Nélaton in 1865. In Germany, the first operation was made by Guster Simon in 1876, and he was followed by Langenbeck the following year. In 1884, Bruns found 33 recorded cases, and in 24 of this number the result was satisfactory. As a rule, sensation returned gradually in from two to four weeks, while motion did not return until three weeks to three months after the operation. Complete restoration of function was seldom completed until half a year to one year after the operation. As in cases which require secondary suture the nerve-ends are sealed with a mass of cicatricial tissue, it is always necessary to resect the ends, after which the sutures are applied in the same manner as in primary nerve suture. Both nerve-ends must be freed from all cicatricial adhesions before approximation is attempted, and, if this cannot be readily done on account of previous retraction, both ends are carefully stretched and sufficient elongation secured so as to prevent any tension upon the sutures. A great deal can be done to prevent tension, by placing the limb in such a position as will relax the nerve; for instance, flexion of the hand and forearm in suturing the ulnar, median, or musculo-spiral, and flexion of the leg and extension of thigh after reuniting the sciatic. The position of the limb most favorable for the union of a sutured nerve is best secured by a plaster-of-Paris dressing, which is allowed to remain not only till the external wound is healed, but until the nerve has firmly united. When a nerve has suffered at the seat of injury a considerable loss of substance, it is often found impossible to bring their ends in contact by nerve-stretching and position of limb, and in such cases restoration of continuity becomes an exceedingly difficult task.

Létiévant suggested that the defect in such cases should be corrected by a neuroplastic operation. He proposed that a flap should be taken from each end sufficiently long that, when turned toward each other, they could be sutured at the middle of the defect, thus making a connecting bridge of nerve-tissue between the separated nerves. As could be expected, in a case where he performed this operation the result was negative. In a case operated on by Tillmanns after this method, partial restoration of function was established three and a half months after the operation. The success in this case was probably not the result of conduction of nerve force along the fibres of the flaps, but the production of new fibres across the gap, perhaps through the tissues composing the temporary bridge. From his experiments on animals, Gluck came to the conclusion that nerve defects could be corrected by transplantation of nerves; that is, inserting a piece of nerve from an animal, corresponding in size to the nerve to be reunited, between the nerve ends, and uniting it with them with sutures. He reports a number of successful experiments on chickens, filling the gap with a nerve taken from rabbits. Philipeaux and Vulpian, from their own researches, came to the conclusion that a transplanted nerve always degenerates and disappears, and that restoration of structure and function only takes place by regeneration from the nerve-ends., It is probable that the methods of nerve restoration devised by Létiévant and Gluck are useful in reuniting separated nerve-ends in the same manner as the *suture à distance* of catgut suggested by Assaky. The interposition of an aseptic, absorbable substance like catgut or nerve-tissue serves as a temporary scaffolding for the products of tissue proliferation from the nerve-ends, which at the same time determines the direction for the new material, providing the shortest route to meet the same material from the other side. When catgut is employed, two or three sutures are used, so that the combined size of the strings will at least approximately correspond to the size of the nerve. Vanlair, who believes that regeneration of a nerve takes place exclusively from the proximal end, resected a piece of the sciatic nerve in dogs, and then sutured both ends of the nerve to the ends of a decalcified-bone tube, which in length corresponded to the section of nerve removed. From the results of his experiments, 10 in number, he became satisfied that continuity of the nerve was restored by the new nerve-fibres from the proximal end growing into the tunnel, bridging the defect in a comparatively short time, as they had no resistance to overcome, and uniting with the end of the nerve on the opposite side of the tube. It appears to the author that this method of overcoming the difficulties of reuniting nerve-ends widely apart is not only an ingenious procedure, but, if applied in practice, promises better results than any other method heretofore proposed. In certain cases where the distal end cannot be found, or where the separation is so great that none of the methods of approximation so far devised hold out any inducements of a successful issue, Létiévant suggested the idea of grafting the central end upon the intact trunk of a neighboring nerve. This operation failed in his hands, but Tillaux and Tillmanns, slightly modifying the method, were successful. In Tillmanns' case the ulnar nerve had been divided, the ends were found separated 4½ centimetres, and the proximal end was grafted upon the median nerve. Sensation returned in a month, and by using electricity and massage recovery was complete a year later. Nerve-grafting, as advocated by Létiévant, should only be resorted to after implantation of a decalcified-bone tube between the nerve-ends has been tried and proved a failure, or in cases where the defect is very extensive, or, finally, if, after the most diligent search, the distal end cannot be found. Restoration of function does not always follow after the continuity of a nerve has been restored by operative measures. Ehrmann has reported such a case. The radial nerve was divided below the elbow and failed to unite. Complete paralysis of all the muscles supplied by this nerve. After the lapse of seven months the nerve was exposed, and the ends, which were 5 centimetres apart, were vivified and sutured. Seven months after the operation, no improvement. The nerve was again exposed at the former site of operation, and it was found that union had taken place, but the nerve was compressed by a firm cicatrix 2 or 3 centimetres in length. The nerve was relieved from its imprisonment, and when the faradic current was applied all the muscles supplied by the nerve responded. Four months later, complete recovery. This case reminds us of the importance of securing healing of the nerve and wound with as little cicatricial tissue as possible, which can only be done by absolute asepsis and careful attention to suturing of the wound.

CHAPTER III.

INFLAMMATION.

THE subject of inflammation is one of deep interest both to the student and practitioner, as it initiates the former into the field of general and special pathology, and the latter meets with it daily in some form in his practice. We have already set apart from inflammation those numerous processes by which injuries or defects are repaired without destruction of any of the new tissue-elements which have been described in the first chapter under the head of Regeneration. From a scientific and practical stand-point, it is exceedingly important to draw a distinct line between the series of tissue changes which attend regenerative processes, uncomplicated by the action of pathogenic bacteria, and true inflammation, *which is always caused by the presence of one or more kinds of pathogenic microbes.* As compared with true inflammation it has been customary for quite a number of years to speak of regeneration as a plastic or regenerative, inflammatory process; but the term *inflammation* in the future should be limited to the series of histological changes which ensue in the living body from the presence and action of specific micro-organisms, while the word *regeneration* should be used to designate the histological changes which take place in tissues which have been primarily in an aseptic condition or have been rendered so after the inflammation has subsided. From this it will be seen that the study of inflammation is intimately and inseparably associated with a consideration of the new science of bacteriology. For most forms of inflammation the presence of a specific micro-organism has been demonstrated, and its etiological relationship established by cultivation and inoculation experiments; and in the few inflammatory diseases where no such positive proofs can be furnished we have, from analogy and circumstantial evidence, reason to suspect the presence of undiscovered microbes. Inflammation, in the widest and most comprehensive meaning of the word, should be made to embrace pathological conditions which are caused by the action of pathogenic microbes or their ptomaines upon the histological elements of the blood and the fixed tissue-cells. A correct definition of inflammation, which should embody the etiological, anatomical, and pathological characteristics of the disease from our present knowledge of the subject, cannot be given, as many important points connected with the complicated processes await explanation by future investigation. Sanderson defines inflammation as "*the succession of changes which occur in a living tissue when it is injured, provided that the injury is not of such a degree as at once to destroy its structure and vitality.*" As we have restricted the term inflammation to *the succession of changes which occurs in a living tissue* from the action of pathogenic microbes or their ptomaines, this definition would cover processes which, for reasons already given, we have considered as instances of tissue proliferation unattended by any of the characteristic features of inflammation. J. Bland Sutton uses the term inflammation in a more restricted sense in coining the following definition: "*It is the method by which an organism attempts to render inert noxious elements introduced from without or arising within it.*" As nothing is said of the *method*, the most important part of the definition, it certainly cannot be said to cover the whole ground. The conception of the true nature of inflammation for the present, at least, must remain symptomatic. As a rule, inflammation subsides as soon as the primary cause has disappeared or has been rendered inactive, as is well shown by the spontaneous disappearance of febrile disturbances in the general infective diseases, and the subsequent rapid repair of the local lesions which characterize them. If an acute inflammation become chronic, either from a diminution of the quantitative or qualitative intensity of the primary cause, or from the tissues becoming accustomed to its action, it is sometimes difficult to tell whether the primary cause has disappeared or has ceased to act, or whether it is still present and active. In chronic inflammation the most reliable indications of the presence and potency of the primary bacterial cause are acute exacerbations, as chronic inflammation only consists of *a series of acute inflammatory processes which repeat themselves at larger or shorter intervals.* The differences between an acute and chronic inflammation are not in kind, but in degree. The complicated processes which characterize inflammation can be studied most profitably by considering separately and conjointly the symptoms to which they give rise, which Galen enumerated as *calor*, *rubor*, *dolor et tumor*, to which may now be added the *functio læsa* of modern authors. The study of the objective and subjective manifestations of inflammation should be preceded by a short description of

THE HISTOLOGICAL ELEMENTS WHICH ARE DIRECTLY CONCERNED IN THE INFLAMMATORY PROCESS.

Capillary Vessels.—The most important histological changes in inflammation, acute or chronic, transpire within, and in the immediate vicinity of, capillary vessels. The smallest arteries and veins, the vessels on either side of the capillaries, undergo changes, and the disturbance of circulation within them constitutes a part of the picture of inflammation, but it is in the capillaries that the most serious disturbances occur; it is here where the *noxæ* are brought in closest contact with the para-vascular tissues, and it is here where the inflammatory exudation and transudation take place. The capillaries are minute vessels, or rather channels, which connect the arteries and veins, the walls of which are composed of a thin, elastic, endothelial membrane; that is, a single layer of nucleated cells held together by an amorphous cement-substance. In silver-stained specimens the cement-substance appears as dark lines which outline the boundaries of the cells.

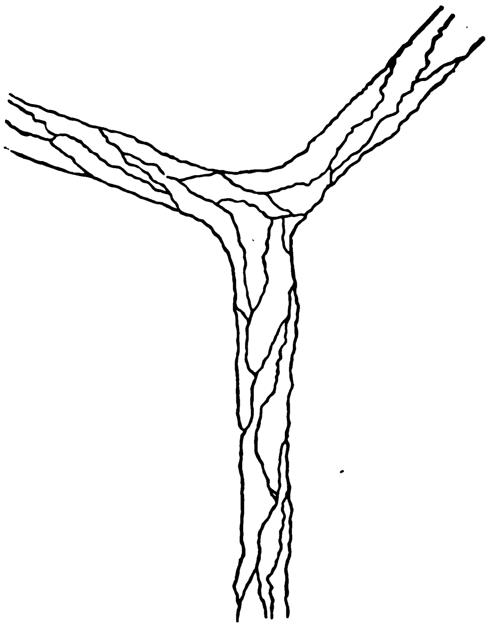

FIG. 30.—CAPILLARY VESSELS OF THE FROG'S MESENTERY, STAINED WITH NITRATE OF SILVER ONLY; THE WALL OF THE VESSEL IS VIEWED FROM THE SURFACE, AND IS SEEN TO CONSIST OF ELONGATED ENDOTHELIAL CELLS, MARKED BY THEIR OUTLINES ONLY; THE NUCLEUS OF THE INDIVIDUAL CELLS IS NOT SHOWN. (*Klein.*)

The shape of the cells is more or less elongated, with pointed extremities, and their outline smooth or sinuous. The nuclei of these cells are oval, situated either about the middle of the cell or near one extremity. The nucleus contains within a well-defined membrane a net-work of chromatin threads, but no nucleolus. When the capillaries undergo alteration and distention, as in inflammation, the cement-substance yields in many places; in consequence of this minute openings appear, called by Arnold *stigmata*, which become gradually enlarged into *stomata.*

Winiwarter found that by injecting inflamed capillaries the contents of the vessel escaped through these openings. Through these openings emigration of leucocytes takes place, and when the inflammation is very intense the red corpuscles escape,—a process which Stricker has named *diapedesis*. If the capillary vessels, through which emigration has been going on, be stained with nitrate of silver, it is seen that the emigration is limited to the interstitial cement-substance of the endothelial wall. (Purves.)

Klein has shown that the walls of all capillary vessels in the adult state form a direct connection with the process of the connective-tissue corpuscles of the surrounding tissue,—a matter of great interest in studying the relationship between the capillary vessels and the surrounding connective-tissue spaces.

Blood-corpuscles.—The blood-corpuscles frequently serve as carriers of the microbic cause of the inflammation; they block the lumen of inflamed capillary vessels, partially or completely, and constitute the histological elements of the primary exudation. The element of the blood which is more intimately associated with the histology of inflammation is the

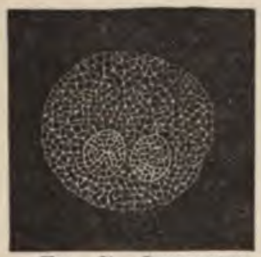

FIG. 31.—LEUCOCYTE, SHOWING RETICULUM OF PROTOPLASMIC STRINGS. (*Klein.*)

I. Leucocyte, or White Blood-corpuscle.—This is a nucleated, spherical, transparent mass of protoplasm, without a limiting membrane or envelope. Heitzmann made the discovery that it is composed of a reticulum of protoplasmic strings, with a hyaline substance in the meshes.

The nucleus shows a similar structure, and its net-work is continuous with that of the cell-body. Stricker and Klein, as well as a number of other histologists, have adopted Heitzmann's views in reference to the minute anatomy of the leucocyte. The reticulated structure is well shown by staining with chloride of gold, which stains the protoplasmic strings, but not the interstitial substance. The leucocyte is endowed with intrinsic power of locomotion,—amœboid movements,—a function which is performed by the reticulum. Wharton Jones discovered motion of protoplasm in leucocytes of human blood as early as 1846. In 1862 Haeckel showed that the white blood-corpuscles absorb pigment-granules, —a process which can only take place by amœboid movements, which by change of form of cell bring the foreign material into its interior by inclusion. These observations enabled Cohnheim to demonstrate later that the white blood-corpuscles found in the vascular spaces of the cornea were derived from the blood; in other words, to establish the fact of emigration of leucocytes through the inflamed wall of capillaries. The amœboid movements of the colorless corpuscles can be well observed for hours in the moist chamber on the warm stage.

The movements of a leucocyte are peculiar. The first effort consists of a protrusion of a hyaline film. This is withdrawn, and another is protruded; in the next moment this is diminished to a very minute process, whereas, on the opposite side, a new, broad process appears. After this the corpuscle is seen to throw out processes of various length and thickness, and thus to alter its shape in a considerable manner. By virtue of the amœboid movement of leucocytes they move from place to place independently of the blood or plasma current. This independent locomotion enables them to pass through the small opening in the wall of inflamed capillaries, and, after they have reached the para-vascular tissues, to travel along connective-tissue spaces until arrested by some mechanical obstruction. If pigment-material, in a finely-divided state, is mixed with blood, either before or after withdrawing it from the vessels, the projections thrown out by the leucocytes inclose the particles brought in contact with it, and the granules reach in this manner the interior of the leucocytes, and are variously distributed according to the shape and movements of the protoplasm. Microbes reach the interior of the leucocytes in the same manner. In cases of intra-vascular infection the emigration corpuscles convey with them the microbes through the wall of inflamed capillaries into the tissues surrounding them.

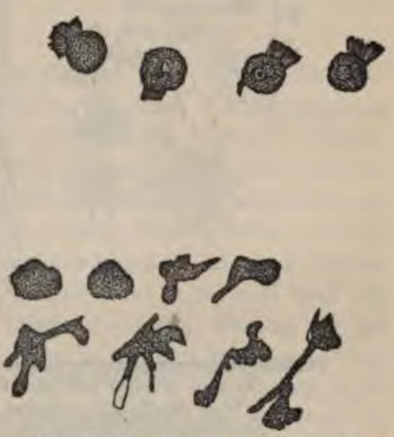

FIG. 32.—CHANGE OF FORMS OF A MOVING LEUCOCYTE BY AMŒBOID MOVEMENTS. (*Klein.*)

2. Red Blood-corpuscle.—The colored blood-corpuscle serves less frequently as a carrier of microbes than the leucocyte, as it does not possess amœboid movements. For the same reason it is not found so constantly as a component part of the inflammatory exudation, as its transit through the capillary wall is entirely a passive process, and is accomplished only by the *vis a tergo* in case the stomata are sufficiently large to permit its passage. The presence of numerous colored corpuscles in the exudation is an indication of great acuity and intensity of the inflammation,—conditions causing serious and extensive alterations of the capillary wall. The escape of whole blood through a capillary vessel greatly damaged by the cause of the inflammation is called *rhexis*.

3. Third Corpuscle.—A third cellular element in the blood, the third corpuscle, was discovered by Max Schultze, in 1865. He described it as a small, colorless sphere or granule. Elaborate descriptions of this corpuscle were given by Hayem, in 1878, and Bizzozero, in 1882. Hayem, from his observations, believed that these minute structures represented young colored blood-corpuscles, and hence named them hæmatoblasts. Bizzozero entered his protest against this theory and called them blood-plates (*Blutplättchen*). Under the microscope they appear as minute, faintly-colored blood-corpuscles. They seem to possess a little stroma like the red blood-corpuscles, but contain no nucleus and are devoid of any cell-membrane. What appears as a nucleus is, according to Hayem, an optical defect.

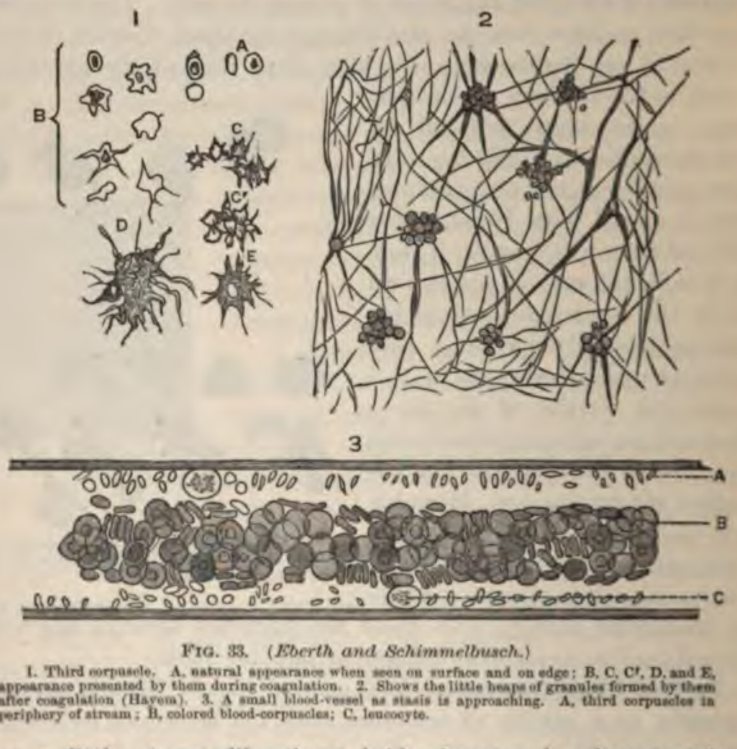

FIG. 33. (*Eberth and Schimmelbusch.*)

1. Third corpuscle. A, natural appearance when seen on surface and on edge; B, C, C', D, and E, appearance presented by them during coagulation. 2. Shows the little heaps of granules formed by them after coagulation (Hayem). 3. A small blood-vessel as stasis is approaching. A, third corpuscles in periphery of stream; B, colored blood-corpuscles; C, leucocyte.

Hayem estimates that they are forty times more numerous in man than the leucocytes, and twenty times more abundant than the colored corpuscles. As there has been no positive proof furnished that the third corpuscle is an embryonal red blood-corpuscle, and as it has been shown that blood-corpuscles are produced from the fixed cells of blood-producing organs, as, for instance, the spleen and medullary tissue, it is advisable not to apply to it the term hæmatoblasts, but to designate it from the remaining two morphological elements of the blood numerically by calling it the third corpuscle. Under a higher power the third corpuscle can be readily recognized in the blood-stream of capillary vessels in the mesentery or web of a frog. In blood withdrawn from a vessel it is destroyed as soon as coagulation sets in; hence it disappears almost immediately after it leaves the blood-vessel. In order to study it outside of the body, means must be employed to prevent coagulation, which can be done by mixing the blood with the following solution, recommended by Hayem:—

Distilled water, ...	200.00 cubic centimetres.
Sodic chloride, ...	1.00 gramme.
Sodic sulphate, ...	5.00 grammes.
Mercury bichloride, ...	0.50 gramme.

From a needle-puncture the blood is allowed to mix with the solution in the proportion of about 1 to 20 up to 1 to 100. In this mixture the third corpuscle will retain its shape and size for twelve to twenty-four hours. The third corpuscle is a fibrin-producing structure, and, as such, it takes an active part in the formation and growth of intra-vascular blood-clots. The white mural thrombus, produced *intra vitam*, is composed almost exclusively of this element of the blood. If, from a trauma or disease the endothelial lining of a blood-vessel is injured and the smooth surface becomes uneven, the third corpuscles, floating in the peripheral portion of the axial current, come in contact with projecting points, and are arrested and become attached to the vessel-wall, layer after layer is added, and in this manner the mural thrombus is formed. On the surface of recent wounds they appear in large numbers, lose their fibrin ferment, and give rise to the formation of fibrin, which acts both as a hæmostatic and temporary cement-substance. In inflammation the third corpuscle escapes through the capillary wall in the same manner as the red corpuscles, but, on account of its smaller size, its peripheral location in the blood-stream, and its greater abundance, it is numerically more abundant in the inflammatory exudation. The fibrin in inflamed tissues is undoubtedly derived largely from this source.

4. Fixed Tissue-cells.—The fixed tissue-cells behave differently in the inflamed part, according to the intensity and nature of the primary microbic cause. The microbes, or their ptomaines, may possess such intense local toxic properties as to destroy their vitality directly when the inflammation results in necrosis, as is the case in the centre of an ordinary furuncle, and on a larger scale in cases of progressive phlegmonous inflammation. The fixed tissue-cells may be destroyed by starvation, by the primary inflammatory exudation being so abundant as to obstruct the circulation in the inflamed part. If the cause of the inflammation is less intense, as is the case in chronic inflammation, the fixed tissue-cells are brought in direct contact with the microbes which produced the inflammation, and active tissue proliferation is the result, and this furnishes the bulk of the inflammatory product. The histological structure of tubercle furnishes a good illustration of the part taken by the fixed tissue-cells in chronic inflammation. In chronic suppurative inflammation the fixed tissue-cells are first transformed into embryonal tissue, and, as the protoplasm of the new cells is destroyed by the ptomaines of pus-microbes, they are converted into pus-corpuscles. A passive rôle in the inflammatory process was assigned to the fixed tissue-cells by Boerhave, who regarded stasis as the essential feature of inflammation; by Andral, who believed that hyperæmia was the characteristic pathological condition in an inflamed part; and by Rokitansky, who taught that exudation constituted the most important element in all inflammatory lesions. Virchow located the primary seat of inflammation in the fixed tissue-cells, and asserted that nutritive or formative irritation occurred in them independently of vessels or nerves. He maintained that the more the cells were disposed to take up nutritive material the greater the danger that they themselves would be destroyed. Remaining faithful to the doctrine that inflammation is only caused by the presence and action of a specific microbic cause, we shall find that the more acute the process the less the probability that the fixed tissue-cells take an active part, and that the more chronic the inflammation the greater the amount of the new material that has been derived from the fixed tissue-cells, and the smaller the quantity of vascular exudation.

SYMPTOMS OF INFLAMMATION.

The structural changes caused by inflammation give rise to a characteristic complexus of symptoms,—pain, redness, swelling, heat, and suspension,—elimination or perversion of function. These symptoms vary in intensity, according to the nature of the primary cause and the anatomical structure and location of the tissues affected. One or more of the symptoms enumerated may be absent, when the existence of inflammation must be ascertained by a more careful study of those presented. In acute inflammation the symptoms appear in rapid succession or almost simultaneously, while in the chronic form they come on slowly, often almost insidiously, and frequently one or more are wanting, even when the disease which those that are present represent is far advanced. The number and intensity of the individual symptoms vary not only according to the virulence of the primary microbic cause, but are also modified by the resisting capacity of the individual and the tissues affected. We speak of a complete or partial immunity to certain microbic diseases, and of a general or local, hereditary or acquired, disposition. For diagnostic purposes the symptoms must be studied individually and collectively, and with special reference to their etiology and the location and structure of the inflamed tissues or organ.

(a) **Pain.**—Pain is one of the most variable symptoms of inflammation. It is caused by traction or pressure to which sensitive nerve-filaments are subjected in the inflamed tissues, and probably also, in some instances at least, by extension of the inflammatory process to the structure of the nerves themselves. Some patients are more sensitive to pain than others. The same extent and degree of inflammation of the same part giving rise to sensation of discomfort in a torpid person may cause excruciating pain in patients with a nervous temperament. As the degree of pain will depend largely upon the number of sensitive nerves present in the inflamed area and the amount of exudation, we would naturally expect to find pain a prominent symptom in inflammations of unyielding tissue freely supplied by sensitive nerves. This, as a rule, is the case. Pain is a distressing symptom in cases of phlegmonous inflammation of the fascia and tendon-sheaths of the fingers and palm of the hand. Pain is the most conspicuous symptom in periostitis and inflammation of the serous membranes. Wherever the inflammatory exudation appears rapidly in parts freely supplied with sensitive nerves, pain from tension appears as one of the foremost symptoms, and continues without intermission until tension is relieved. In acute suppurative osteomyelitis intense pain is present from the very commencement of the disease, and continues unabated until tension is removed by operative procedures, or by the escape of inflammatory product, through some defect in the bone, into the more yielding paraperiosteal tissues. The pain is throbbing, sometimes synchronously, with the pulse in acute circumscribed phlegmonous inflammation. It is sharp and lancinating in inflammation of serous membranes. It is described as a burning sensation in inflammation of the skin. The pain is of a dull, aching, boring character in deep-seated inflammation, especially in the interior of bone. Nocturnal exacerbation of pain is a common occurrence, and seldom absent in painful syphilitic affections. The pain is not always referred by the patient to the seat of inflammation, as in the early stages of coxitis it is not in the hip, but over the inner aspect of the knee, and in inflammatory affections of the nerves the pain radiates along the peripheral branches, and is usually felt most severely some distance from the seat of the disease. In ascertaining the existence and exact location of a deep-seated inflammation, tenderness is a more valuable symptom than spontaneous pain. Tenderness is the pain elicited by pressure. If the inflamed part is tender on pressure and accessible to palpation, the area of tenderness will correspond to the extent of the inflammation. During the beginning of an attack of phlegmonous inflammation the surgeon is able to locate the affection accurately, by searching for the point where the tenderness is most acute, and the same symptom will indicate to him, earlier than any other, the direction in which the process is extending. In periostitis the area of tenderness will show whether the inflammation is circumscribed or diffuse. The existence of circumscribed points of tenderness about the epiphyses of the long bones is almost a certain indication of central osseous tuberculosis, and, at the same time, furnishes a reliable guide in their early operative treatment. Firm pressure relieves pain in nervous hysterical patients, while it aggravates it when it is caused by inflammation. On the other hand, superficial pressure made with the tips of the fingers increases the suffering in parts the seat of functional disturbance, while it does not materially affect the pain resulting from inflammatory lesions.

(b) **Redness.**—The composition of normal blood is admirably adapted for the passage of this fluid through capillary vessels. As long as the relation of corpuscular elements to the blood-plasma remains normal, and the intima of the blood-vessels remains intact, and the *vis a tergo* is adequate, there is no tendency to capillary obstruction. If the capillary circulation in the mesentery of a frog is examined under a microscope, there is no difficulty in distinguishing two currents,—the axial and peripheral. The axial or central current is rapid and conveys the red corpuscles, which have the same specific gravity as the blood-plasma, while the peripheral current between the axial and vessel-wall is considerably slower, and in this current the colorless corpuscles are conveyed, their rotating motion being due to their coming in contact with the wall of the vessel. D. J. Hamilton has shown, by numerous experiments, that in fluids holding in suspension solid particles passing through capillary tubes the heaviest particles are carried along the central current, while those specifically lighter than the fluid seek the peripheral current. The leucocytes are specifically lighter than the fluid in which they are contained; hence they are forced into the space between the axial current and the vessel-wall (Fig. 33, C). The third corpuscle, probably for the same reasons, moves also in the peripheral stream. The colorless corpuscles accumulate more in the peripheral stream when the current is feeble than when it is rapid. This fact is of great importance in the study of the altered circulation when the capillary vessels are in a state of inflammation. The accumulation of colorless corpuscles in the peripheral stream in inflamed capillary vessels, according to Thoma, Eberth, and Schimmelbusch, is owing to the slowness of the current, which, although insufficient to propel the specifically light, colorless corpuscles, is still competent to force onward the less-resisting and specifically heavier-colored corpuscles.

Eberth and Schimmelbusch state that in the vessels of a warm-blooded animal four kinds of stream are noticed, in accordance with its velocity: (1) the normal stream, in which the axial current and peripheral zone are readily recognizable; (2) a slow stream, in which the leucocytes accumulate in the periphery; (3) a still slower stream, in which the third corpuscles also leave the axis and accumulate in the periphery, and in which, these observers assert, the leucocytes become less numerous; and (4) a stream so slow as to approach stagnation, in which all the elements of the blood are indiscriminately mixed. From the above it can be seen that all general and local conditions which tend to diminish the velocity of the blood-current in the capillary vessels are productive of accumulation of the colorless corpuscles and of the third corpuscle in the peripheral stream,—a condition which greatly aggravates the existing local impediments to capillary circulation, and when well advanced, by encroaching more and more upon the central stream, will result in complete stasis. Redness as a symptom of inflammation signifies an excess of blood in the part, and the terms used to indicate its existence are hyperæmia and congestion, while complete arrest of the capillary circulation is expressed by the word *stasis*. Accurately speaking, *hyperæmia* should be used to designate that condition of the circulation where the part not only contains an increased amount of blood, but where an increased amount of blood flows *to* and returns *from* the part,—an exalted physiological process; while the word *congestion* literally means only an accumulation of blood in a part,—a condition owing to some form of local or distant mechanical obstruction. The condition giving rise to redness, hyperæmia, congestion, and stasis should not be studied only from descriptions, but in order to be understood they should be seen. This can be readily done by producing artificially an inflammation in a transparent part of some lower animal, preferably the frog, and studying the circulation in the inflamed part step by step under the microscope. For this purpose experimenters have usually selected the frog's web, mesentery, tongue, lung, and bladder, and the tadpole's tail. For general use the frog's web should be selected, as the preparations for this experiment are very simple. Inflammation is provoked by cauterizing the web with a needle heated to a red heat, or by applying with a small plug of cotton some powerful irritant, as ammonia, tincture of cantharides, or croton-oil, or by touching the surface with a sharp stick of nitrate of silver. Hamilton gives the following directions for making the experiment: "Nothing more is necessary than a piece of tin or other soft metal, about $1\frac{1}{2}$ to 2 inches broad and about 6 to 8 inches long, or, what is better, a thin piece of hard wood of the same dimensions. At the end where the web is to be stretched it should not be so broad. From the narrow end of this a V-shaped piece is cut out, over which the web is to be spread. The frog should first be curarized, as this does not interfere with the circulation, provided that the solution employed be not too strong. The $\frac{1}{5000}$ of a grain, in watery solution, injected under the skin, is sufficient. Chloral may be substituted. Caton recommends a solution of 4 grains to the drachm. As many minims should be injected subcutaneously as the

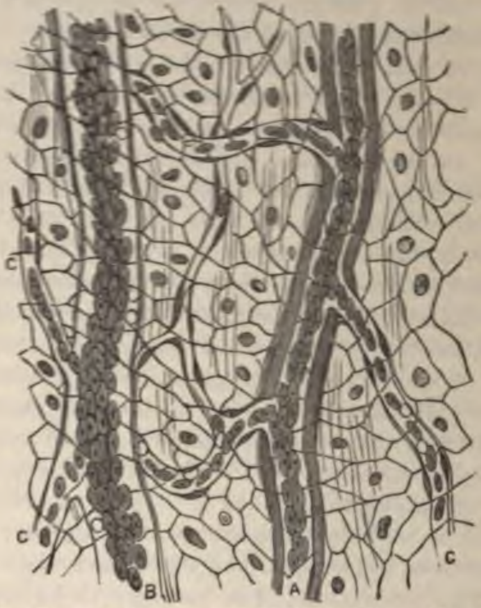

FIG. 34.—NORMAL CIRCULATION IN FROG'S WEB. (*Landerer.*)
A, artery; B, vein; C, capillaries. Vessels covered by a net-work of polygonal epithelial cells of web, in which pigmented cells are not represented.

frog is drachms in weight. The injection is made under the skin of the back with an ordinary hypodermic syringe. The animal is laid on the piece of metal or wood, and, the web being stretched over the cleft at the end, the toes are held by tying a piece of thin thread to them and fixing the ends into a fine slit cut in the metal or wood." The microscope is so arranged and adjusted that the field of observation will correspond to the point of irritation. A sufficiently high power is used so that the different corpuscular elements in the capillary stream can be readily seen and recognized. In order to witness the different stages of the inflammatory process it is necessary to continue the observation for hours.

Any one of the irritants mentioned applied to the frog's web will produce in the capillaries over a limited area a series of changes which are always present in inflammation, and a description of them will represent what takes place in capillaries the seat of inflammatory process of bacterial origin; almost simultaneously with the application of the irritant a momentary contraction of the vessel occurs, caused by the stimulation of the vaso-contractor nerves, which is followed by dilatation, with increased velocity of the capillary current,—a true hyperæmia. The bright-red color of the hyperæmic part at this stage, according to Recklinghausen, is due to increase in the rapidity of the blood-current, but, as the color of the blood indicates a diminished expenditure of oxygen and a smaller quantity of carbon in the blood, increased velocity alone would not explain this change. Diminished alkalescence in the inflamed tissues may reduce the amount of oxygen used, as is the case in glands during active secretion, where Claude Bernard showed that defective oxygenation is always present. At this stage the corpuscular elements circulate in their respective streams, and the whole picture is one of increased physiological activity. Dilatation of the vessels follows contraction so quickly that it would be difficult to explain it as a para-

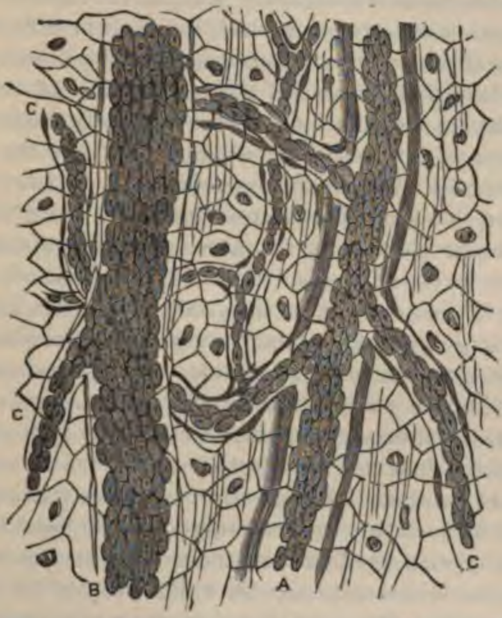

FIG. 35.—CAPILLARIES OF FROG'S WEB IN A STATE OF HYPERÆMIA SOON AFTER APPLICATION OF IRRITANT. (*Landerer.*)

A, artery; B, vein; C, capillaries.

lytic phenomenon. Its early outset and the rapidity with which it appears would point to a neurotic cause, traceable to the action of ganglia in the vessel-wall. It has not yet been satisfactorily explained whether this early dilatation of the vessel is due to vasomotor paralysis or irritation of the vaso-dilators, but it is more probable that it is caused by the vaso-dilators, while, later, paralysis from overdistention occurs. Division of the sympathetic in the neck brings about increased vascularity, but no inflammation. The difference between dilatation of an inflamed vessel and the dilatation following division of the sympathetic consists in alteration of the capillary wall, in the former instance produced by the action of the causes which induced the inflammation, while in the latter the dilatation is a purely nervous phenomenon, unattended by other pathological conditions of the vessel-wall. Disturbances of the circulation alone are not sufficient to bring about the local changes which are characteristic of inflammation; if the velocity of the blood-current is greatly diminished by purely mechanical or nervous causes, mural implantation of the white corpuscles may take place, but emigration does not occur on account of the absence of the essential condition which gives rise to it,—alteration of the capillary wall.

Dilatation is first noticed in the smallest arteries, afterward in the veins and capillaries, and keeps increasing from fifteen minutes to two hours. The vessels often enlarge to double their normal calibre. During the stage of dilatation many of the capillaries which were small or contained but little blood become visible, which greatly adds to the turgidity and redness of the inflamed part. As long as the acceleration of the capillary current continues, the different corpuscles move in their respective currents. The white corpuscles that are mingled with the colored are washed along with the latter in the central stream without finding their way into the slower side-current which propels the leucocytes and the third corpuscles. The leucocytes in the peripheral stream appear more numerous, and skip along by more rapid rotatory movements. At this time the circulation has reached its greatest speed, and the tissues present every appearance of well-marked hyperæmia. In from fifteen minutes to two hours from the time the irritant was applied, intra-vascular changes are noticed which are calculated to impede the capillary current. The first link in the chain of local causes which obstruct the capillary circulation consists of a crowded condition of the vessels from a greater accumulation of the different corpuscles, which is soon followed by a greater separation of the leucocytes from the central current and their greater accumulation in the peripheral stream, where they often become arranged in heaps and little masses. This change is first observed in the small veins, and somewhat later, and to a lesser extent, in the smallest arteries. Separation of the blood-corpuscles is the necessary outcome of slowing of the stream from greater accumulation. In the peripheral zone of leucocytes the next source of obstruction is created. Some of the colorless corpuscles become momentarily attached to the capillary wall, when they are again detached by the force of the current, or are rolled away by another leucocyte. As the process advances it appears as though the viscosity of the leucocytes was increasing constantly, as more and more of them become adherent, while fewer are again detached. The lumen of the vessel is narrowed more and more by mural implantation of the leucocytes. The small veins now assume an appearance as if the internal surface of their wall were paved with leucocytes, while in the capillaries a similar adhesion of the leucocytes to the wall is noticed. At this stage it often appears as though complete obstruction would occur every moment, the capillary stream becoming completely arrested for a moment, and the current may even move in an opposite direction, when the obstruction is again overcome and the current moves once more in the right direction. The smallest arteries exert themselves to the utmost to clear the way, and pulsations can be seen where in a normal condition they are absent. Hyperæmia has now given way to congestion. An intra-vascular obstruction has given rise to accumulation of blood on the proximal side of the inflamed vessel. Increasing slowing of the current gives rise to greater accumulation of leucocytes, which become firmly adherent to the capillary wall, narrowing the vessel more and more until the space for the axial current becomes too small for the passage of the red corpuscles, when complete arrest of the circulation takes place. Congestion has resulted in stasis. As soon as complete stasis has taken place the colorless corpuscles become mixed with the red corpuscles which are forced into the mass of the white, while by amœboid movements the latter wander toward the centre of the vessel and mix freely with those which were moving in the central current. The most advanced stages of vascular disturbance are, of course, noticed first where the irritant was applied, so that when complete stasis has taken place in the centre a zone of congestion surrounds this, while more distant vessels still present every indication of active hyperæmia. Redness is most marked where hyperæmia is extant; that is, in parts containing a maximum amount of arterial blood. As soon as congestion sets in, the blood-corpuscles, red and white, do no longer pass through the vessel with the same rapidity and number, and the redness gives way to a bluish tinge, which becomes well marked and does not give way to pressure when complete stasis has occurred. The blood in the stagnated vessels, according to Paget, has little tendency to coagulate; hence the possibility of *resistutio ad integrum* of the circulation after subsidence of the acute symptoms. Complete stasis occurs first in such capillaries where the *vis a tergo* is greatly diminished by a circuitous route from an artery to a vein, and increases in the direction in which the blood-current is slowest. In warm-blooded animals the phenomena of inflammation do not differ materially from those observed in the frog's web, except as regards the presence and disposition of the third corpuscles. According to Eberth and Schimmelbusch, in warm-blooded animals the third corpuscles in the normal capillary circulation move along with the colored corpuscles in the axial current, and hence they maintain that they must be of nearly the same specific gravity. A few of the leucocytes, mixed with the colored corpuscles and the third corpuscles, are found in the central stream, but the majority of them are propelled by the peripheral stream, which, according to those observers, is from ten to twenty times slower than the central or axial current. With the slowing of the stream from alteration of the capillary wall and subsequent intra-vascular conditions, separation of the corpuscles takes place in the same manner as has been described in the frog's web; the leucocytes and third corpuscles leave the central stream and accumulate in the slower peripheral zone of capillary stream, where they give rise to a greater degree of slowing of the column of blood by the formation of intra-vascular obstruction, which, if sufficient in degree, finally arrests the central current, thus causing stasis. The inflammatory process in warm-blooded animals can be studied advantageously in the artificially-inflamed omentum of young animals, especially the guinea-pig, as the omentum in these animals is exceedingly delicate and transparent. The animal is narcotized by injecting subcutaneously 3 grains of hydrate of chloral for a full-grown animal. As the animal, with the exception of the head, is to be kept immersed in a physiological solution of salt kept at a temperature of the body in a large vat with a glass bottom, it is wrapped in a sheet of gutta-percha tissue long enough to overlap the head, and made so as to inclose a funnel-like space through which it may breathe. An opening is made in the covering at a point corresponding to the abdominal incision, through which the omentum is withdrawn. The object-glass of the microscope is immersed in the solution, and the omentum laid over a slide without fastening it. The vat is made so that it will fit on to the stand of an ordinary microscope, so that the light can be readily adjusted. Two tubes, one to convey the salt solution into the vat and another to conduct it away, are attached at opposite sides. These can be connected with a vessel whose temperature is kept constant by means of a thermostat and Bunsen burner.

(c) **Swelling.**—The primary swelling in inflammation is due to dilatation of blood-vessels, and its degree will depend on the vascularity of the part inflamed. The more numerous the blood-vessels, the greater the swelling from this cause. As the inflamed blood-vessels will often dilate within two hours to double their normal calibre, the primary swelling in vascular organs in a state of acute inflammation will come on quickly, and will give rise to a not inconsiderable enlargement of the inflamed part. If during this stage of inflammation the tissues are incised, hæmorrhage is profuse, and the emptying of turgid blood-vessels by this means has a prompt effect in diminishing the swelling. Nancrede has shown by his investigations that local depletion, during the hyperæmic stage of inflammation, exercises a favorable influence in unloading the distended blood-vessels and in modifying the intensity of the subsequent conditions in the inflamed tissues. It is also during this stage that the application of cold proves a beneficial resource in the treatment of acute inflammation, as under its effects the distended blood-vessels contract, and in consequence of the diminution of the vascularity of the inflamed part the primary inflammatory swelling is diminished.

I. Inflammatory Exudation.—A moderate amount of swelling is present in all regenerative processes, as dilatation of the vessels necessarily precedes the increased physiological activity of the tissue, and the embryonal material required in the reparative process occupies a larger volume than the mature tissue it is intended to replace. Inflammation is characterized by the presence of a superabundance of cells. The cause which has produced the inflammation has, by its direct action upon the capillary wall, produced such alterations of its structure as to render it more porous, hence permeable to the passage of the inclosed cellular elements of the blood. The albuminous cement-substance which holds together the endothelial cells disintegrates at different points, and through these small defects, the stigmata and stomata, the blood-corpuscles find their way through the capillary wall into the surrounding lymph and connective-tissue spaces. In acute inflammation the inflammatory exudation consists principally in the extra-vascular accumulation of blood-corpuscles which have passed through the injured capillary wall. The rapidity with which the inflammatory exudation appears will depend on the intensity of alteration of the capillary wall and the speed with which the blood-corpuscles escape into the surrounding tissues. In chronic inflammation exudation takes place slowly, and the histological elements of the inflammatory swelling are derived mostly from the fixed tissue-cells.

Emigration of Leucocytes.—The passage of a leucocyte through a defect in the capillary wall is called emigration,—the wandering of such a cell from a place where it has a normal existence into a territory where, in a condition of health, it is seldom met with. After it has made its escape from the capillary vessel it is called an emigration or wandering corpuscle. John Hunter came very near being the discoverer of emigration of leucocytes during his researches on inflammation. He incised the tunica vaginalis in animals, and inserted a tallow plug, which he removed after short intervals, and examined the fluid upon its surface under the microscope. He found in this fluid, a short time after the incision was made, round, white cells, which could have been nothing else but wandering leucocytes.

The credit for having demonstrated the porosity of the capillary wall and the escape of the colorless corpuscles unquestionably belongs to Waller. This author observed emigration in the tongue of the frog as early as 1846, and strongly maintained that the inflammatory exudates were composed largely of leucocytes, in opposition to the blastema theory of formation of pus and other inflammatory products.

In 1849 Addison clearly pointed out the relationship of the colorless corpuscles and the corpuscles lying around the vessel in inflamed parts, as becomes evident from the following sentences from his work on "Consumption and Scrofula:" "During inflammation—using the word in the general sense here indicated—there is more or less marked increase of the colorless elements and protoplasm in the part affected. At first—in the first stage—these elements adhere but slightly along the inner margin or boundary of the nutrient vessels, and are therefore still within the influence of the circulating current, belonging, as it were, at this period as much, or rather more, to the blood than to the fixed solid. Secondly—in the second stage—they are more firmly fixed in the walls of the vessels, and, therefore, now without the influence of the circulating current. Thirdly—in the third stage—new elements appear at the outer border of the vessels, where they add to the texture, form a new product, or are liberated as an excretion."

Recklinghausen found wandering corpuscles in the vascular spaces of the cornea, but he believed that they were a product of tissue proliferation from the fixed corneal corpuscles. Our modern knowledge of emigration of leucocytes is founded almost exclusively upon the labors of Cohnheim. This observer demonstrated, in the year 1867, by his own ingenious experiments, that the wandering corpuscles discovered by Recklinghausen in the vascular spaces of the cornea were leucocytes which had escaped from capillary vessels and had wandered into the cornea. He based his statements on the results of an experiment which could leave no room for discussion. He injected finely-divided pigment-material directly into the circulation of an animal, and somewhat later produced artificially a keratitis. In examining the cornea he found the vascular spaces nearest the margin of the cornea crowded with leucocytes loaded with pigment-granules. There could be only one conclusion,—that the leucocytes, which had become charged with pigment-granules in the general circulation, had passed through the capillary vessels at a point nearest the seat of irritation; in other words, the capillary vessels which took part in the traumatic keratitis furnished the primary inflammatory exudation. A slight irritation of a frog's webb will only produce an active hyperæmia, and in a short time the circulation returns to normal without any emigration of leucocytes having taken place. In such cases the irritant has been of such a nature or of such mild action as not to produce the necessary alteration of the capillary wall for mural implantation and emigration to take place.

Zahn has shown that if the mesentery of an animal is exposed, but carefully protected against injury, emigration of leucocytes does not take place for seven or eight hours, while the remaining disturbances of the circulation indicate the existence of inflammation. If, however, the frog's web or tongue is cauterized with a sharp-pointed pencil of nitrate of silver the necessary conditions for an acute inflammation are created, and the minute eschar is soon surrounded by vessels showing the different stages of the inflammatory process, from active hyperæmia to complete stasis. Emigration of leucocytes takes place most actively in capillaries partly obstructed by mural aggregation of these elements, and the process is arrested as soon as the circulation has come to a complete standstill. The following conditions must be present and are essential for emigration of leucocytes: 1. Alteration of capillary wall. 2. Mural implantation of leucocytes. 3. Permeability of lumen of capillary vessel. 4. Amœboid movements of leucocytes.

1. Alteration of capillary wall has been repeatedly enumerated as the most important feature of inflammation, and without such a change the rapid escape of leucocytes as we find it in inflammation would be utterly impossible. The cause which has produced the inflammation produces such a degree of softening in the cement-substance as to enable its penetration by the leucocytes between the endothelial cells, or, as some of the authors claim, localized minute defects cause the formation of small openings through which the leucocytes escape.

2. Mural implantation of leucocytes is an equally essential condition, as without it the leucocytes, which are at any rate larger in circumference than the supposed openings through which they escape, would be rolled over these minute defects by the sluggish peripheral stream, and emigration would not take place. Increased adhesiveness or viscosity of the leucocytes is supposed to play an important part in the occurrence of mural implantation. According to Hering, mural fixation of the leuco-

cytes is effected by fine projections, which are thrown out on their surface, and which insinuate themselves into the small crevices of the roughened intima. Mural implantation cannot take place as long as the capillary stream retains its normal velocity; hence, slowing of the peripheral current is the first and most important cause. The slower the peripheral stream, the more readily does mural implantation occur, and the greater the tendency to aggregation of leucocytes along and near the capillary wall. The rapid transudation of the plasma of the blood through the defective capillary is undoubtedly another cause of impediment of progress and final adhesion of leucocytes to the inner surface of the capillary vessel. Finally, mural fixation of leucocytes is effected by the changed condition of the protoplasm of the leucocytes and the inner surface of the capillary wall by the action of the essential cause which produced the inflammation.

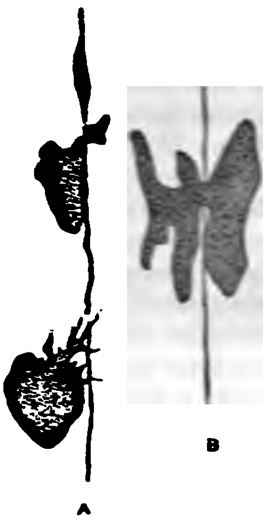

FIG. 36.—LEUCOCYTE PASSING THROUGH CAPILLARY WALL. *Landerer.*

A, leucocyte attached to capillary wall by fine processes; higher up it has penetrated the capillary wall by a large projection. B, half of the leucocyte outside of the capillary wall dragging the balance after it.

3. It has been shown that emigration of leucocytes is most active where the capillary circulation has become impeded, but not arrested, and that the process is arrested with the occurrence of complete stasis; hence, it appears that the intra-vascular pressure is one of the factors in this process. Hering and Schklarewsky maintained that the leucocytes are entirely passive structures in their passage through the capillary wall, that they are forced through defects in the wall exclusively by the intra-vascular pressure. That emigration is not such a simple process is evident, as there would be in such case a larger representation of colored corpuscles in the inflammatory exudation. The blood-pressure assists in the extrusion of leucocytes that have penetrated the capillary wall, but, without changes in their form, would not be adequate to force them through the minute openings or the softened cement-substance.

4. Leucocytes, in order to pass through an inflamed capillary wall, must possess amœboid movements; hence, only living leucocytes are capable of migration.

After the leucocyte has become implanted upon the inner surface of the capillary wall it penetrates the softened cement-substance by throwing out projections, or one of these projections insinuates itself into one of the minute foramina, and as the intra-mural portion increases in size the balance of the leucocyte is drawn toward it; this step is greatly aided by the blood-pressure, which pushes the intra-vascular portion in the direction of the growing projection, until by its own exertions, and aided by the *vis a tergo*, it has finished its journey through the capillary wall, and has reached the para-vascular lymph or connective-tissue spaces, where it constitutes the most important element of the inflammatory exudation. In the inflamed capillaries of the frog's web, under the microscope, this process of emigration can be readily followed, and leucocytes can be seen in the same field in various stages of transit through the wall, and finally liberated in the para-vascular spaces. Frequently one leucocyte after another can be seen passing through the same place,—a fact which points strongly to the existence of well-defined circumscribed defects in the capillary wall. As the escaped leucocytes accumulate outside of the capillary vessels, some of them can be seen to change their location by the same forces which have been active in their passage through the vessel-wall,—amœboid movements and stream of parenchyma fluid.

Diapedesis.—This word was devised by Stricker to designate the passage of colored corpuscles through the inflamed vessel-wall. If there could be any doubt as to the existence of minute openings in the inflamed capillary wall in the consideration of emigration of leucocytes, this doubt must be effectually dispelled when the passage of colored corpuscles through the capillary wall can be demonstrated under the microscope. Experimental research and clinical observation have shown that when the inflammatory action is very intense red corpuscles form no inconsiderable part of the inflammatory exudation. As the colored corpuscles possess no amœboid movements, their passage through the capillary wall must be an entirely passive process; they are extruded through preformed openings or through an exceedingly soft cement-substance by the intra-vascular pressure. It is possible that they are forced through passages made by the emigration corpuscles. It is well known that at first only leucocytes are found outside of the capillary vessels, that the colored corpuscles appear later, and that, while leucocytes also pass through the smallest veins, the colored corpuscles escape only through capillary vessels (Fig. 37, D).

Arnold noticed that red corpuscles floating in the capillary stream, when they arrived opposite a stomata, were drawn toward the opening of the transudation stream.

Diapedesis becomes a prominent feature where the inflammatory process is very acute, consequently where extensive alteration of the vessel-walls has taken place. In such instances the colored corpuscles are so numerous in the exudation as to impart to it a hæmorrhagic appearance. An abundant escape of colored corpuscles in inflammation is technically called *rhexis*. The third corpuscles are extruded through the inflamed capillary wall in the same passive way as the colored corpuscles.

The primary inflammatory exudation consists of the corpuscular elements of the blood which escape through the porous capillary wall, the products of their disintegration, and blood-plasma. The latter will be again referred to under the head of Transudation. The presence of the solid constituents of the blood differentiates the inflammatory exudation from an ordinary hydropic or œdematous swelling. The question rises, What becomes of the corpuscular elements after they have left the general circulation? The most favorable termination of the inflammatory process consists in the preservation of the vitality of the cellular elements outside of the blood-vessels and their return into the general circulation by a process which is called immigration. This probably seldom, if ever, takes place in the case of the colored and third corpuscles, both of which possess no amœboid movements and undergo molecular disintegration, and the granular detritus is removed by absorption. The leucocytes which have retained their vitality can return into the circulation either by re-entering the capillaries which they have left,

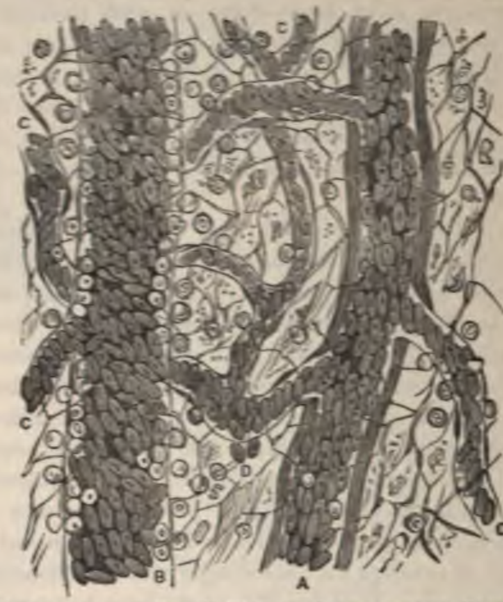

FIG. 37.—INFLAMMATION OF FROG'S WEB AT STAGE WHERE CAPILLARY STREAM IS IMPEDED BY COMMENCING EMIGRATION. (*Landerer.*)
A, small artery; B, small vein; C, capillaries; D, red corpuscles which have escaped from capillary by diapedesis.

after the acute symptoms have subsided and the capillaries have been cleared of the mural thrombi, or by a more indirect route through the lymphatic vessels. The latter route is probably the most frequent. If the blood-corpuscles contain the microbic cause of the inflammation in sufficient quantity and intensity to destroy their protoplasm, they furnish the necessary nutrient medium for the growth and development of the microbe outside of the vessel-wall, thus bringing it in direct contact with the para-vascular tissues, which then become the seat of infection. In such instances the cellular elements of the primary inflammatory exudation are dead tissue, and act or are disposed of as such. In acute suppurative inflammation the leucocytes which have escaped are converted into pus-corpuscles. *The emigration corpuscle under no circumstances assumes a tissue-producing function.* When inflammatory processes result in the formation of new tissue, this function is performed by fixed tissue-cells which have been stimulated to a state of activity by the increased nutritive conditions incident to some form of inflammation. The albumen, which is always present in considerable quantity in every inflammatory exudation, furnishes an additional nutrient supply, and thus assists the process of cell proliferation; this is especially the case with the globulins. The filtrate which percolates through the inflamed capillary wall contains coagulable substances, which, in hydropic fluids, are less abundant. The emigration corpuscles, which disintegrate soon after they have left the capillary vessels, furnish fibrin ferment. Fibrin production in the tissues is suspended as soon as the product of emigration has become copious. The third corpuscles furnish another source of fibrin production. In suppurative inflammation fibrin formation does not take place. Where no fibrin forms in the exudation, the supposition lies near that the fibrin-producers are taken up by the cells, or that the fibrin which had already been produced is liquefied and assimilated by them. If the inflamed vessels are surrounded only by a few leucocytes, the latter are destroyed and liberate fibrin ferment; if abundant, they are more resistant and destroy albuminous substances. Weigert asserted that cell necrosis resulted in the formation of fibrin, as the dead cells furnish the fibrin ferment. That fibrin production does not always attend inflammation can only be explained by the supposition that the fibrin-producers are assimilated as soon as they have left the blood-channels. If the cells which furnish the fibrin come in contact with necrotic tissue, such an assimilation is prevented and fibrin is formed. Fibrin production, however, may take place without cell necrosis, as is the case upon inflamed serous surfaces. Its occurrence in this particular locality can only be explained by the absence of assimilation of the cells which yield the fibrin ferment. The cellular constituents and fibrin of the inflammatory exudation impart to it one of its characteristic clinical features,—a sense of firmness,—which is well marked in proportion to the predominance of these over the fluid portion.

Inflammatory Transudation.—The liquid portion of the blood which escapes through the damaged wall of inflamed capillary vessels is called inflammatory transudation. The same causes which are necessary to extrude the non-amœboid corpuscular elements of the blood constitute also the conditions which enable a part of the blood-plasma to leave the capillary stream. Increased porosity of the capillary wall is the most important of them. As soon as the capillary wall has become abnormally permeable the blood-pressure forces the fluid through the minute pores into the surrounding connective tissue, or, if the inflammation is located in a mucous or serous membrane, upon the surface. In deep-seated inflammation the transuded fluid freely percolates through the connective-tissue spaces, and gives rise to one of the well-known symptoms of inflammation,—the *inflammatory œdema.* The transudation is always more widely diffused than the exudation. Recent bacteriological researches have shown that, while in the tissues, at the seat of exudation, the presence of the microbic cause of the inflammation can be readily demonstrated by microscopical examination and cultivation experiments, the œdema fluid some distance from them was found free from micro-organisms. The escape of blood-plasma in inflammation is a process which resembles percolation through a porous membrane. As the blood-plasma contains fibrinogen and fibrino-plastic material, its presence in the tissues or upon inflamed serous or mucous membranes is important in the production of fibrin. In some instances the inflammatory product is greatly changed by the presence of a copious transudation, and the inflamed part then presents more the appearance of œdema than inflammation. This is well shown by the two clinical varieties of anthrax. The expression *serous inflammation* is used to indicate the predominance of transudation over exudation in some forms of inflammation. The liquid transudate predominates over the exudate in some forms of suppurative inflammation (purulent œdema of Pirogoff), also when the circulation is feeble, as in the aged and in anæmic individuals. The addition of mucus alters the character of an exudation or a transudation, as may be seen when a mucous membrane is the seat of inflammation. Serous transudation often precedes mucous exudation, as in cases of acute catarrhal inflammation of the nasal passages. After the acute symptoms of inflammation have subsided and the capillary circulation has been restored, the transuded fluid is absorbed, and with its absorption the inflammatory œdema disappears. In suppurative inflammation the transudation becomes the pus-serum.

(d) **Heat.**—Increase of temperature of the inflamed part is the result of increased afflux of blood and the accompanying augmentation of physiological processes. Cohnheim showed experimentally that inflammation, without an increased blood-supply, does not give rise to an increase of temperature. John Hunter was already aware that the temperature at the seat of inflammation is never in excess of the temperature of the blood. Heat is both a subjective and objective symptom. In acute inflammation of the skin, or a mucous membrane, the patient often complains of a distressing burning or scalding sensation, which is often effectually relieved by cold applications. The surface thermometer is sometimes an important instrument in setting a differential diagnosis between a deep-seated chronic inflammation and a malignant tumor. Diminution of temperature may indicate either a favorable change or complete arrest of circulation in the inflamed part, in the first instance showing that resolution is in progress, in the latter commencing the speedy occurrence of gangrene.

(e) **Disturbance of Function.**—As inflammation, wherever it occurs, consists essentially of increased nutritive changes in the tissues, resulting in consequence of a more abundant blood-supply and an exaggerated vegetative capacity of the cells, it may lead to at least a temporary increase of function. This is always the case in inflammation of mucous membranes, where, as one of the prominent clinical features, we observe an increased secretion of mucus usually preceded and accompanied by a more or less profuse transudation. Parenchymatous inflammation in glands usually produces sudden diminution and often complete suppression of secretion. Acute suppurative osteomyelitis is attended by almost complete suspension of all the functions of the affected limb. Myositis arrests the contractility of the muscles affected. The pain caused by an inflammation may interfere with the functions of adjacent organs, as may be seen in the fixed chest-wall in cases of acute pleuritis, and in fixation of the abdominal walls, with diminished or suspended respiratory movements of the diaphragm, in cases of peritonitis. The accumulation of inflammatory products may prove a serious obstacle to important functions, and often constitutes a direct cause of death, as in cases of intra-cranial inflammation, where death is more frequently caused by compression of the brain than destruction of the contents of the cranial cavity; and the accumulation of serum or pus in the pleural cavity or pericardium, where a fatal termination can often be traced to mechanical causes from the presence of a copious effusion. Diminution of function often affords the earliest indication of the existence of a deep-seated chronic inflammation, as is evident from the slight limp which ushers in a coxitis or the imperfect flexion and extension in chronic inflammation of joints other than the hip-joint.

CHAPTER IV.

INFLAMMATION (*continued*).

MODIFICATION OF INFLAMMATION BY THE ANATOMICAL STRUCTURE AND LOCATION OF THE INFLAMED TISSUE.

THE clinical course and pathological conditions of inflammatory processes are materially modified not only by the primary cause, but also by the anatomical structure and location of the inflamed tissues. Inflammation of serous or mucous surfaces has a tendency to spread in a peripheral direction, and, as a rule, remains superficial, and the exudation and transudation are poured out in the direction offering the least resistance; that is, upon the free surface. In tissues that are dense and unyielding the swelling, for physical reasons, is limited, and the inflammatory products give rise to tension, which may arrest the circulation completely and cause necrosis, as is the case in acute suppurative osteomyelitis. When the area of inflammation is supplied with an abundance of connective tissue the swelling often attains enormous dimensions in a short time, as may be seen in every case of phlegmonous inflammation of the deep-seated connective tissue of the extremities, neck, chest, and abdomen. Acute inflammation of organs that are exceedingly vascular gives rise to an early and abundant exudation, as can be demonstrated in every case of croupous pneumonia and acute nephritis. Inflammation of non-vascular tissue is accompanied by the formation of new blood-vessels, which grow in the direction of the seat of inflammation from the nearest vascular district. Some tissues are more disposed to inflammation than others; thus, the connective tissue is more frequently the seat of acute inflammation than muscles, and the medullary tissue than the bone-substance proper, and most causes which give rise to chronic inflammation are known to select certain organs and tissues in preference to others.

PARENCHYMATOUS INFLAMMATION.

In the study of the cardinal symptoms of inflammation special attention was given to the part taken in the inflammatory process by the capillary vessels and the blood-corpuscles. Alteration of the capillary wall was alluded to as the most important pathological condition, as upon it depends the emigration of the corpuscular elements of the blood and the occurrence of the inflammatory transudation, which together constitute the primary inflammatory swelling. Incidentally it was stated that as soon as the cause which gave rise to the inflammation is brought in direct contact with the fixed tissue-cells, these take part in the inflammatory process and contribute their share to the inflammatory exudation. Inflammation is said to be parenchymatous when the parenchyma of an organ is the primary seat of inflammatory changes, as when the secreting structures of a gland are implicated from the beginning. In all such instances the blood-vessels which furnish the vascular supply have undergone the characteristic changes which have been described, and with few exceptions the microbes have been conveyed to the parenchyma through them. The cloudy swelling of parenchyma cells is either an evidence of the existence of degenerative changes, or it denotes the beginning of coagulation necrosis from the specific effect of pathogenic microbes upon their protoplasm. A cloudy appearance of cells is one of the first manifestations of the presence of a parenchymatous inflammation. Lesion of connective tissue or parenchyma cells is next to alteration of capillary wall, and emigration of blood-corpuscles the most important pathological condition of inflammation, and, as far as the ultimate result is concerned, the most important, as extensive destruction of parenchyma cells will result in suspension of function, and death of the organ affected is one of vital importance. As soon as the fixed tissue-cells outside of the vessel-wall have become implicated their physiological resistance is diminished,—a condition which cannot fail in aggravating the existing vascular disturbances. Landerer maintains that the normal elasticity of the tissues surrounding the capillary vessels is an essential factor in preserving the equilibrium between the intra-vascular pressure and the surrounding tissues in a normal condition of the circulation. This mechanical theory of inflammation is founded upon the supposition that this normal elasticity of the para-vascular tissues is diminished by the causes which give rise to inflammation, and that when this has occurred the capillary walls have lost their outer support, in consequence of which they become dilated, and hyperæmia, slowing of blood-current, emigration, and transudation follow as the result of purely mechanical causes. Ingenious as this theory may appear, it cannot explain the complicated processes which characterize inflammation. The train of pathological conditions which attend inflammation must be regarded as effects of a common microbic cause upon the capillary wall, their contents, and the fixed tissue-cells outside of the capillary vessels. In parenchymatous inflammation the cause has reached the parenchyma cells, either directly, as when microbes are brought in contact with a mucous surface, become attached to and penetrate the parenchyma cells, multiply in their interior, and, later, reach the connective tissue and blood-vessels, or, what is more common, the microbes reach the parenchyma through the circulation. In both instances the capillary vessels and the connective tissues between them and the parenchyma cells take an active part in the inflammatory process. The microbes may be present in such great number or may possess such intensely virulent properties as to destroy the parenchyma cells, as is the case in diphtheritic inflammation of mucous membranes. When less intense in their action the parenchyma cells proliferate, and the embryonal cells, being less resistant, succumb later, as when suppuration occurs in the parenchyma of an organ, or they remain indefinitely in their embryonal state, as can be readily verified by examining the different forms of chronic inflammatory swellings,—the so-called granulomata.

INTERSTITIAL INFLAMMATION.

In this form of inflammation the connective tissue is the seat of cell emigration and tissue proliferation. Many of the microbes select the connective-tissue spaces; they locate and multiply here, and the inflammatory product is composed almost exclusively of emigration corpuscles and embryonal connective-tissue cells. Tubercle and gummata present such a histological structure. Phlegmonous inflammation represents the acute form of connective-tissue inflammation. If the connective tissue of an organ become the seat of an inflammatory hyperplasia the parenchyma suffers, either in consequence of pressure or, later, from cicatricial contraction and the inevitable diminution of blood-supply incident to this condition. Parenchymatous inflammation of an organ is preceded or followed by interstitial inflammation, and a primarily interstitial inflammation sooner or later involves the surrounding tissue by direct extension of the inflammatory process, or indirectly the mechanical causes; hence, as a rule, it is anatomically and even etiologically not always possible to differentiate between these two forms of inflammation, nor is such a distinction of much practical importance.

HÆMORRHAGIC INFLAMMATION.

A few colored corpuscles escape through the capillary wall in almost every case of acute inflammation, but their presence in the exudation can only be determined by the use of the microscope. When they are present in sufficient number to impart to the exudation a bloody tinge, we speak of a hæmorrhagic exudation or transudation. A hæmorrhagic transudation into the pleural, pericardial, or peritoneal cavity usually indicates the existence of a tubercular or malignant disease of the respective serous membranes. In cases of acute inflammation with hæmorrhagic exudation, the quantity of the effused blood will be a sign by which we can at least approximately estimate the extent of alteration of the capillary wall. Rhexis can only take place when the capillary wall at some point has been completely broken down and an opening of considerable size has formed through which a small stream from the axial current can escape. Aside of the nature and intensity of the primary cause of the inflammation, hæmorrhagic inflammation is more likely to be met with in persons debilitated from other diseases, in the aged, and in patients suffering from diseases which obstruct the circulation, such as valvular disease of the heart, cirrhosis of the liver, emphysema of the lungs, and chronic affections of the kidney. The presence of blood in a transudation or exudation is always a grave sign, and as such should always be taken into careful consideration in rendering a prognosis.

SUPPURATIVE INFLAMMATION.

In suppurative inflammation at least a part of the exudation is transformed into pus. Transformation of the cellular portion of the exudation, the leucocytes and embryonal cells, into pus-corpuscles is due to the destructive effect upon their protoplasm of the pus-microbes and their ptomaines, while the transudate becomes the pus-serum. Suppurative inflammation occurs either as the result of a primary or secondary infection with pus-microbes. In primary infection with pus-microbes the leucocytes most remote from the blood-vessels, and which have been exposed longest to the specific action of the pus-microbes and their ptomaines, are converted first into pus-corpuscles, while the fixed tissue-cells are first transformed into embryonal cells before the same cause, by destruction of their protoplasm, changes them into similar structures. In suppurative inflammation due to secondary infection, the pus-microbes act upon embryonal cells which owe their origin to an antecedent infection with another microbe of milder pathogenic qualities, as can be seen when tubercular granulations or a gumma undergo suppuration. Suppurative inflammation, in all of its aspects, will be fully considered in the chapter on Suppuration.

INFLAMMATION OF SEROUS MEMBRANES.

Inflammation of the serous membranes has been called exudative, adhesive, suppurative, or serous, according to the character of the inflammatory product. In most inflammatory affections of the serous membranes the surface becomes covered with a copious exudation, which is composed of leucocytes, fibrin, and the products of tissue proliferation of the endothelial and connective-tissue cell. The leucocytes and third corpuscles are rapidly destroyed as they reach the surface, and the fibrin ferment and fibrino-plastic material which are liberated form, on combining with the fibrinogen of the blood-plasma, fibrin. The inflamed membrane is often covered by a thick layer of fibrin, which is firmly adherent to the surface by means of new blood-vessels and granulation tissue which have grown into it. The endothelial cells take an active part in the inflammation, and in case the new product from this source is converted into connective tissue a permanent adhesion forms. In some instances the endothelial cells are destroyed and desquamation takes place, which leaves the subjacent connective tissue exposed. In such cases the superficial dilated capillaries have lost an important support, and transudation takes place freely. D. J. Hamilton has studied

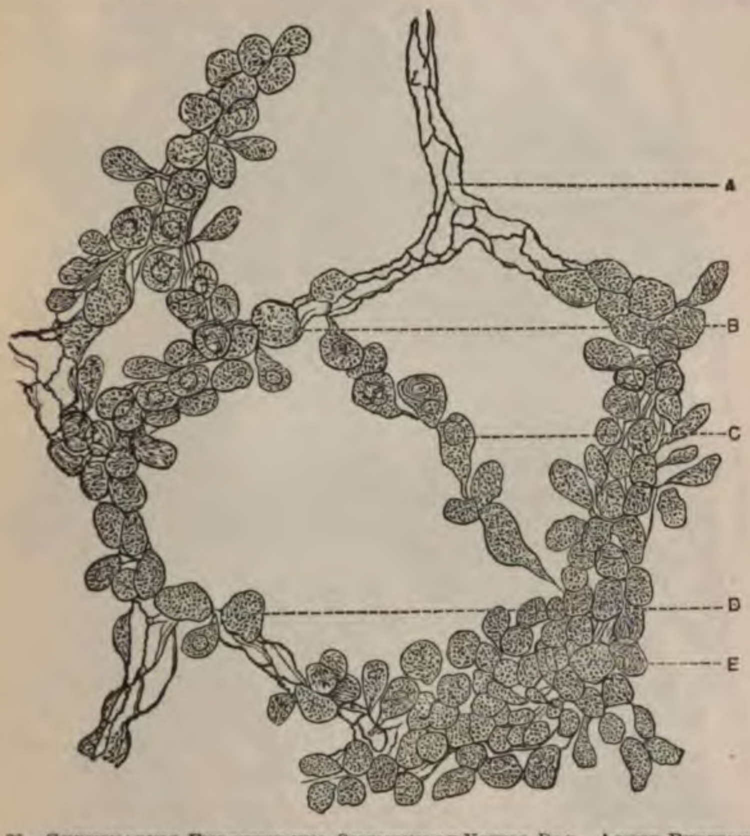

FIG. 38.—GERMINATING ENDOTHELIUM, OMENTUM OF YOUNG DOG. ACUTE PERITONITIS. SILVER-STAINING, × 350. (*Hamilton.*)

A, natural endothelium covering wall of a mesh; B, D, endothelial cells beginning to germinate; C, a chain of germinating cells extending across a fenestra; E, mass of germinating endothelial cells.

the histological changes which occur in periostitis by producing this disease artificially in young dogs. Besides desquamation, he has seen the endothelial cells multiply by division of the nucleus.

The new cells resemble the ordinary granulation or embryonal cells. The connective tissue between the endothelial lining and the blood-vessels

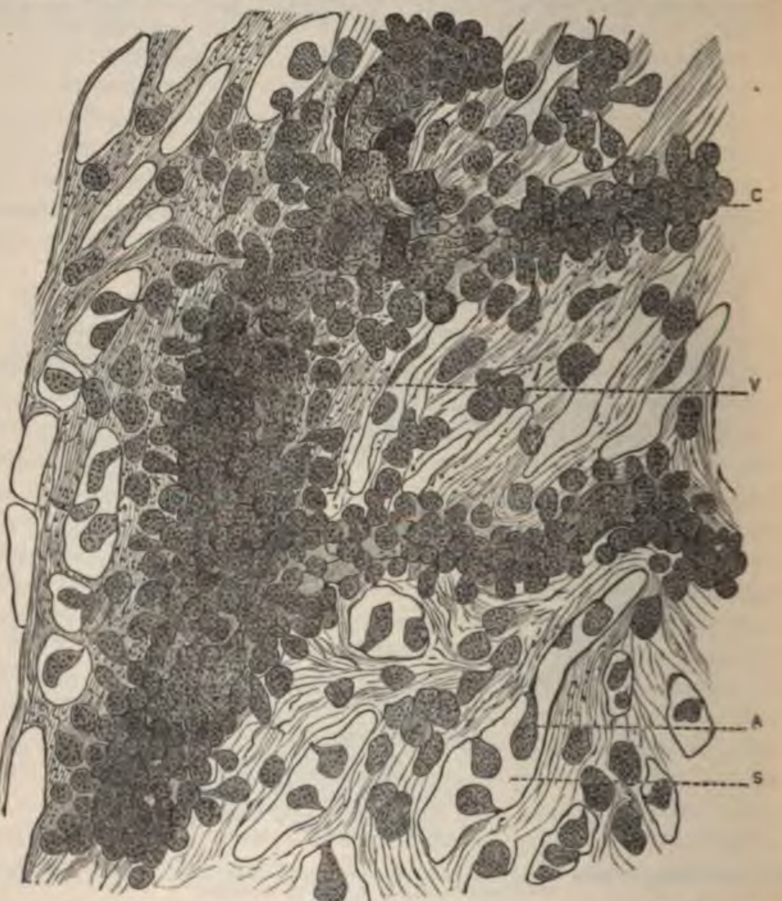

FIG. 39.—OMENTUM OF YOUNG DOG, EXPERIMENTALLY INFLAMED. × 450. (*Hamilton.*)

A, pyriform cell, probably of endothelial origin, sprouting from wall of a fenestra (S) of the membrane; C, capillary, surrounded by extravasated leucocytes; V, small vein, in similar condition.

undergoes tissue proliferation, and the new cells reach the surface and mingle with those derived from the endothelial lining, so that the inflamed surface becomes covered with a layer of granulation tissue. The granulations, accompanied by dilated or new blood-vessels, penetrate into the fibrinous exudation, which is removed in the same manner as a thrombus in a blood-vessel undergoing obliteration. Permanent adhesions and obliteration of serous cavities are affected by the granulation tissue, which removes the inflammatory exudation and establishes an organic union between opposing inflamed membranes. If the fixed tissue-cells do not participate actively in the inflammatory process, the exudation becomes absorbed in the course of time, and the endothelial lining is repaired; thus the temporary adhesions are removed, and the normal relations existing between the serous membrane and inclosed viscera are restored. The blending of the corpuscular elements of the inflammatory exudation of a serous membrane with the product of tissue proliferation of the endothelial cells is well shown in Fig. 39.

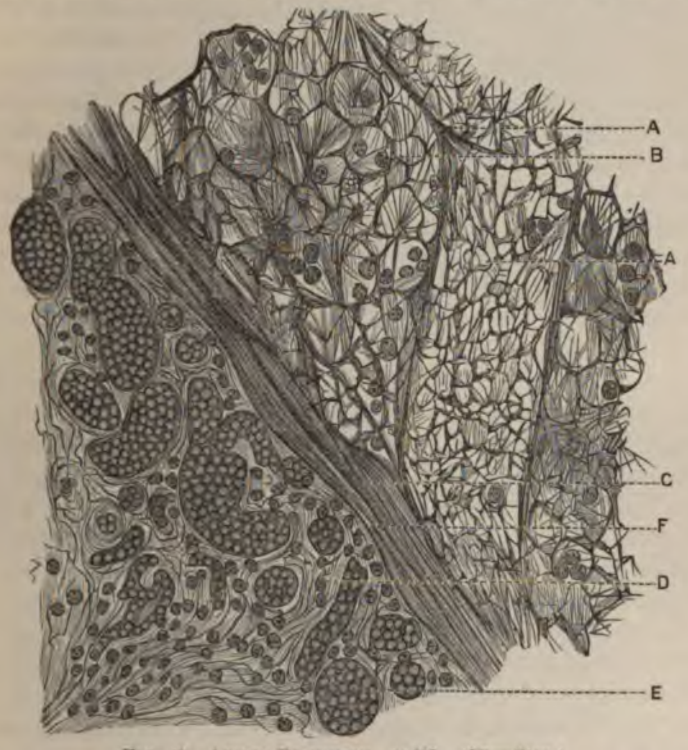

FIG. 40.—ACUTE PLEURISY. × 300. (*Hamilton.*)

A, A, net-work of fibrin; B, an effused leucocyte; C, laminæ of fibrin lying adjacent to the pleura (F); D, small round cells effused into the pleura; E, distended blood-vessel of the superficial layer of pleura.

The pathological anatomy of acute inflammation of a serous membrane at an early stage is well represented in Fig. 40.

The scarcity of leucocytes in the fibrin in the specimen represented by this illustration was undoubtedly due to their rapid destruction as soon as they reached the surface, which resulted in the formation of a copious deposit of fibrin. The round cells in the subpleural connective tissue are effused leucocytes. Sufficient time does not seem to have elapsed for any marked changes to have occurred in the fixed tissue-cells. In suppurative inflammation of a serous membrane, if life is sufficiently prolonged, the leucocytes and embryonal cells are transformed into pus-corpuscles, and in this manner empyema, pyocardium, and purulent peritonitis are produced. The introduction of pus-microbes in sufficient quantity into the abdominal cavity, the power of absorption of which has been reduced by an antecedent affection or an accompanying trauma, will produce such a rapidly fatal peritonitis that the peritoneum, on post-mortem examination, will show little, if any, macroscopical lesions. Death in such cases results from acute septic infection. When life is prolonged for several days, the post-mortem reveals all the evidences of a fibrino-plastic peritonitis; that is, numerous adhesions between the intestines and the parietal peritoneum and among the intestinal loops. In purulent peritonitis the exudation often breaks down as the leucocytes contained in it are converted into pus-corpuscles. Tubercular peritonitis is usually attended by a copious exudation, which limits the process and encapsulates the serous transudation. If, in an inflammation of a serous membrane, the transudation predominates over the exudation, the character of the process is indicated clinically by a subacute or chronic course and the absence of severe symptoms. Hydrothorax often develops insidiously, and perhaps the first subjective symptom is difficulty of breathing. Tubercular peritonitis with copious circumscribed effusion has been frequently mistaken for ovarian cyst, not only because the swelling closely resembles a unilocular ovarian cyst, but also from the absence of any of the usual local symptoms which attend the usual forms of fibrino-plastic peritonitis. It appears that the causes which give rise to the form of inflammation of serous membranes do not act with sufficient intensity on the capillary wall and the para-vascular tissues to provoke a copious exudation and active tissue proliferation, but create conditions which permit a copious transudation to take place. It has been recently a much-discussed question whether or not all cases of serous effusion into the chest are of tubercular origin. The fact remains that many cases of subacute and chronic pleurisy die subsequently from tuberculosis, and the natural conclusion would be that the disease was primarily caused by a localized tubercular focus, which, at the time, could not be detected. It is evident that the causes which produce serous transudation do so not only by producing changes in the capillary wall which permit free transudation, but also by bringing about alterations which diminish or completely suspend the power of absorption; hence, not only the occurrence of transudation, but accumulation of the liquid effused. The presence of blood in the transudation is usually an indication of the presence of tuberculosis, carcinoma, or sarcoma.

INFLAMMATION OF MUCOUS MEMBRANES.

Inflammation of a mucous membrane represents another variety of surface inflammation which is greatly modified by the anatomical character of the tissue the seat of the inflammatory process. We have seen that inflammation of serous membranes presents as its most characteristic pathological feature a plastic exudation on its surface, composed of the exuded blood-corpuscles and the products of their disintegration, which are firmly attached to the endothelial lining, which in part has been destroyed and detached by desquamation, while the cells which have retained their vitality proliferate new tissue, which mingles with and ultimately removes the exudation. The epithelial cells which line mucous membranes when in a state of inflammation are stimulated to increased activity, and consequently secrete an increased quantity of mucus, which is the characteristic pathological and clinical feature of

I. CATARRHAL INFLAMMATION.

Inflammation of a mucous membrane is called catarrhal as long as the product consists of an increased secretion of mucus. If a part of the mucous lining is destroyed and the discharge becomes a mixture of pus and mucus, it is no longer proper to call it a catarrhal inflammation, as the pus-microbes have wrought changes that bring the process within the legitimate sphere of suppurative inflammation. Catarrhal inflammation produces a thickening of the mucous membrane by infiltration of the submucous tissue, which, if copious, may subsequently give rise to cicatricial contraction, and, if the inflammation is located in a tubular organ, to the formation of strictures. According to Virchow, a catarrhal inflammation may lead to the formation of superficial ulcers,—the so-called catarrhal ulcers.

II. SUPPURATIVE INFLAMMATION.

In this form of inflammation of a mucous membrane, the leucocytes which are extruded upon its surface, as well as the embryonal cells, are destroyed by the pus-microbes and are converted into pus-corpuscles, which, when mixed with the mucus secreted by the cells which have retained their physiological function, form the muco-purulent discharge. Most of the ulcers which form upon mucous surfaces result from circumscribed necrosis or suppurative inflammation. A catarrhal inflammation very frequently precedes the suppurative form, and a circumscribed suppurating area is usually surrounded by a zone of catarrhal inflammation. Cicatricial obliteration of a tubular organ can only take place after extensive defects of its mucous lining from necrotic, ulcerative, or traumatic causes. Limited defects are repaired by regeneration of the epithelial cells, either from the margins of the defect or from remnants of glands. The most frequent causes of ulceration in the intestinal canal are dysentery, typhoid fever, and tuberculosis. Ulcers which result from the sudden obliteration of a small blood-vessel by thrombosis or embolism are met with after extensive burns in the upper portion of the small intestine and in the stomach in chlorotic females. A strange form of perforative enteritis has recently been described by Mikulicz. A similar case was operated on in the Zurich Klinik, and a careful description of the pathological conditions found at the necropsy has been given by Klebs. He found multiple perforations in a circumscribed portion of the jejunum, and only a few of them had been found and closed by the surgeon who performed the operation. The perforations on the peritoneal side were covered by a plastic exudation. The lumen of the intestine corresponding to the affected portion was considerably enlarged. Mucous membrane not much changed in appearance, but, on close inspection, a number of small defects, partly hidden under the folds, were detected, and were found to correspond with the covered defects on the outer surface. On microscopical examination, it was found that the villi and mucous membrane were softened and denuded of the epithelial lining and infiltrated with cells over a considerable distance beyond the perforations. The most marked changes were found in the submucous tissue, which was also much softened, and the scanty intercellular substance was found traversed by wide spaces in which were found numerous large cells with large oval nuclei. Besides these enlarged parenchyma cells, and in their vicinity, leucocytes which had undergone fragmentation were found. As the capillary vessels were much dilated and in a condition of inflammation, Klebs looks upon the process as a hyperplastic parenchymatous enteritis. As the leucocytes found in the tissues presented all the evidences of fragmentation, there can be but little doubt that this rare form of enteritis presents only another variety of suppurative inflammation of the mucous membrane of the intestine.

III. CROUPOUS INFLAMMATION.

When inflammation of a mucous membrane is attended by the formation of a fibrinous exudation or false membrane upon its surface, it is called croupous. The formation of a fibrinous exudation upon a serous surface, we have found, is always associated with a more or less extensive destruction and desquamation of endothelial cells, and a similar superficial change takes place in croupous inflammation. Weigert states that unless the epithelial surface of a mucous membrane be broken the inflammatory exudation from it will not coagulate. As croupous inflammation of a mucous membrane is probably always produced by direct infection, it is probable that the micro-organisms destroy some of the epithelial cells, and as the inflammatory process penetrates deeper into the tissue, the exudation and transudation coming in contact with dead tissue on the surface, fibrin is deposited, and, becoming entangled with the cellular *débris*, it becomes adherent to the partially-abraded and uneven surface. The fibrin is arranged in layers in the form of a coarse net-work, in the meshes of which is a finer reticulum of the same, with leucocytes and embryonal cells thrown off from the surface. Some membranes contain numerous leucocytes, while in others they are destroyed in the process of coagulation. Separation of a false membrane takes place either by the mucus secreted by intact cells underneath it, or if the mucous lining has been completely destroyed by suppuration and granulation. It has been claimed that, pathologically, a croupous membrane differs from a diphtheritic exudation in that, in the former, the lining of the mucous membrane is found intact after stripping it off, while in a diphtheritic inflammation there is always found a loss of surface substance after removing the membrane. Upon this more apparent than real anatomical difference the discussion on the non-identity of croupous and diphtheritic inflammation rests. As superficial coagulation necrosis is present in all cases of croupous inflammation, and if this process is etiologically different from diphtheritic inflammation, the pathological conditions are different only in degree and not in kind. False membranes, wherever they may form upon a mucous or serous surface, serve as nutrient media for micro-organisms, and the underlying surface is subjected to the risks of recurring infection from them as long as they remain.

INFLAMMATION OF NON-VASCULAR TISSUE.

The importance of blood-vessels in inflammation can be best shown by a study of the pathological conditions in inflammation of non-vascular tissue. The part taken by the blood-vessels and the fixed tissue-cells in the inflammatory process can be most satisfactorily demonstrated in non-vascular organs.

Cornea.—Cohnheim first demonstrated emigration of the colorless blood-corpuscles in artificially-produced keratitis. He cauterized the cornea in animals, and then observed cell infiltration from its margins at a point corresponding to the nearest vascular supply. For the purpose of showing that the cells were not products of the fixed tissue-cells he injected, a few days before the cauterization, finely-divided cinnabar into the circulation, and found that the leucocytes, as they escaped from the capillary vessels, contained granules of the pigment which he had injected. The leucocytes were seen to wander through the vascular spaces of the cornea toward the seat of cauterization. As he could observe no changes in the fixed corneal corpuscles at the seat of cauterization, he maintained that the inflammatory product was derived exclusively from the blood, and that its escape from the blood-stream depended on alteration of the capillary wall. He regarded the dilatation of blood-vessels, which occurs soon after the application of the irritant, as a result of reflex action, and attempted to prove, by specimens of keratitis stained with chloride of gold, that the fixed tissue-cells remained unaffected by the inflammation. Stricker maintained the opposite view, and proved, in silver-stained specimens, that the corneal corpuscles had undergone changes which indicated that they performed an active part in the inflammation. Recklinghausen resorted to a very ingenious experiment to establish his theory regarding the origin of the wandering cells in the vascular spaces of the cornea. He cauterized the cornea of a frog, excised it immediately, and kept it under conditions favorable to cell vegetation, and found, later, wandering cells in the vascular spaces, the origin of which he traced to tissue proliferation of the corneal corpuscles after excision; but even his assistant, F. A. Hoffmann, expressed the opinion that the cells might have been leucocytes which had entered the vascular spaces before the cornea was excised. It is more than doubtful that tissue proliferation would take place in an excised cornea, even under the most favorable physical conditions. There can be no doubt whatever that the primary exudation in traumatic keratitis, as in all other forms of acute inflammation, takes place from inflamed capillary vessels, as Cohnheim has demonstrated so beautifully; but this constitutes only a part of the phenomena which characterize inflammation in the cornea and all other tissues, as, later, the fixed tissue-cells participate in the process, and the new cells derived from them form a part of the inflammatory products. The parenchymatous changes are even more important than the vascular, as repair after subsidence of inflammation is accomplished exclusively by proliferation of the fixed tissue-cells. Eberth has demonstrated, by his accurate histological researches, that the corneal corpuscles near an eschar, made for the purpose of producing a keratitis, multiply by karyokinesis, and regeneration is effected exclusively by the embryonal cells derived from this source. The corneal corpuscles possess a high vegetative capacity, resembling in this respect the connective tissue, to which they bear a strong resemblance, having a similar embryological origin, and receive their nutritive supply through a system of lymph-channels or vascular spaces which are in intimate relationship with the sclerotic vessels at the border of the cornea. The plasma or lymph-channel in the cornea are loosely filled with a liquid albuminoid substance, in which can be seen, even in a normal condition, occasionally a lymph-corpuscle. In artificial keratitis these channels are first packed with leucocytes, which escape from the congested capillaries at the limbus corneæ, enter them directly, and wander toward the seat of irritation far in advance of the new blood-vessels. Infiltration of the cornea with leucocytes gives rise to cloudiness. At first Cohnheim claimed that infiltration of the cornea always occurred from the periphery, but in some of the later experiments on the corneæ of spring frogs he noticed cell accumulation around the central eschar made with a sharp pencil of nitrate of silver, and, as he was absolutely opposed to the idea that the corneal corpuscles could take any active part in the process, he came to the forced conclusion that the cellular elements of the conjunctival fluid were increased, and that these had wandered into the cornea through the lesion at the centre. Stricker has observed karyomitotic changes in the corneal corpuscles surrounding a central eschar as early as three hours after cauterization, and after twenty-four to forty-eight hours cell proliferation was seen to be present all around the inflamed area.

From what different authors have written on the subject of artificial keratitis, which, of course, must be accepted as a fair representative of the clinical forms of this disease, it becomes apparent that the first evidence of inflammation is an increased amount of fluid in the vascular spaces, causing distention and, consequently, swelling of the cornea. As the plasma canals become distended the cells lining them are in part destroyed, and the fluid escapes between two laminæ and forces them partly asunder. (Fig. 41, C, C.) At this time the endothelial cells and corneal corpuscles undergo tissue proliferation, and the new cells form part of the inflammatory product. With the breaking down of the vascular spaces resulting in lymph stasis, accumulation of lymph-corpuscles also takes place, by which another cellular element is added to the inflammatory product. The plasma channels and artificially-formed spaces between laminæ are now blocked with leucocytes, lymph-corpuscles, and embryonal cells. If the irritation is prolonged for a sufficient length of time, vascularization of the inflamed cornea will take place in the course of one or two weeks by the formation of new vessels from pre-existing sclerotic vessels at the corneal border. The new blood-vessels grow in the direction of the seat of irritation, occupying a triangular field, with the apex directed toward the centre, the base corresponding to the limbus corneæ. The vascular portion of such a cornea is called a pannus. In suppurative keratitis the emigration corpuscles undergo fragmentation and are converted into pus-corpuscles; at the same time the embryonal cells exposed to the action of the pus-microbes furnish another histological source for pus production. The fibrous tissue within the suppurating area necroses on account of the disturbed nutrition and the toxic effect of the pus-microbes and their ptomaines, and an abscess results. Vascularization of an inflamed cornea furnishes one of the most beautiful illustrations of the presence of protective resources in the organism, which, when called upon to meet different emergencies, render material aid in the prevention or limitation of destructive processes. Every oculist is familiar with the fact that extensive suppurative keratitis manifests no tendency to reparative action when conditions are present that retard or completely prevent the formation of a pannus. As soon as the process of repair has been completed the new vessels dis-

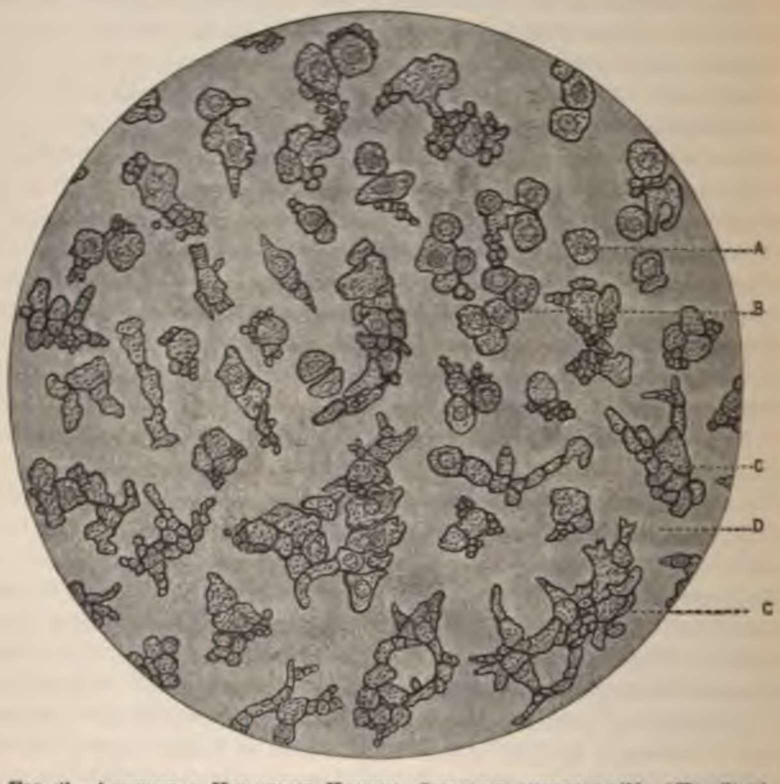

FIG. 41.—ARTIFICIAL KERATITIS, KITTEN. SILVER-STAINING, × 450. (*Hamilton.*)

A, isolated and nucleated cell; B, a group of such still retaining something of the shape of a plasma canal; C, C, plasma canals breaking into fragments; D, the fibrous basis of the lamellæ, or the ground-substance.

appear, leaving a transparent cornea if the defect has been within the limits of the regenerative capacity of the tissues; in case the loss of substance has been too great for complete restoration of structure and function, healing is accomplished by the formation of ordinary cicatricial tissue, which results in the formation of a scar—a permanent opacity of the cornea. In keratitis without suppuration, or attended by a limited ulceration, the cloudiness of the cornea resulting from cell infiltration and the presence of embryonal cells in moderate abundance, transparency is restored with the removal of the wandering cells by granular degeneration and absorption, or their return into the circulation, and the repair of the lesion by the transformation of the embryonal cells into mature, perfect, corneal tissue.

Cartilage.—Cartilage is a structure not only devoid of blood-vessels, but also of any kind of vascular spaces for plasma circulation. Nutrition must here take place by inter- and intra- cellular diffusion of plasma. In its structure it resembles the cornea. On account of the absence of any direct or indirect connection of cartilage tissue with the vessels of the perichondrium all regenerative processes are slow and imperfect, and the inflammatory lesions, which only occasionally are found here as a primary affection, are noted for their chronicity. Artificial chondritis was studied by Goodsir and Redfern. Certain parenchymatous changes were noted at different times after cauterization of articular cartilage. They consist essentially in the enlargement of the cartilage-cells, with increase of the nuclei, or of peculiar corpuscles contained in them, or with fatty degeneration of their contents and fading or similar degeneration of their nuclei. The hyaline intercellular substance at the same time splits up, and softens into a gelatinous and finely molecular and dotted substance. When molecular disintegration or ulceration of cartilage takes place, the enlarged cartilage-cells on the surface are liberated, and the cement-substance disappears in a similar manner after having undergone liquefaction. Küss stated that he had recognized, in articular cartilage under the influence of irritants, certain fibrous transformations, and believed that he had seen, in one case, changes taking place within the cartilage-cells. If articular cartilage be examined in the neighborhood of an ulcerated spot, a complete separation of the fibres, the existence of which in its laminated structure was demonstrated by Thin, by a special method of silver-staining, and its reversion to ordinary white fibrous tissue can be readily made out.

Weber describes new vessels as extending not only over the surface of the ulcerating cartilage, but afterward penetrating its substance. In long-standing ulceration of cartilage a well-marked pannous condition is usually found present, which has resulted from the development of new blood-vessels from the vessels of the perichondrium, which grow in the direction of the inflammatory focus in the same manner as in keratitis. Defects of cartilage caused by inflammation, like defects resulting from a trauma, are only partially repaired on account of the low vegetative capacity of the cartilage-cells, and the product of tissue proliferation is transformed into connective tissue.

PHAGOCYTOSIS.

It has been known for a long time that absorbable aseptic tissues in the living body are capable of removal by the action of certain cells. The absorption of aseptic catgut ligatures by leucocytes and embryonal cells, which accumulate around it and, later, infiltrate it, affords a good illustration of this. Metschnikoff has introduced the term *phagocytosis* to designate a process by which leucocytes and other cells remove dead material and destroy or digest pathogenic micro-organisms. The cells which perform these functions he calls phagocytes. The leucocytes are called mikrophagi, and the fixed tissue-cells, which are capable of performing the same function, makrophagi. Pigment-granules, minute fragments of tissue, and microbes gain entrance into a cell, either by the projections which are thrown out by amœboid cells surrounding and inclosing them (intussusception), or, in the absence of amœboid movements, by a special property of the cells, by which they take up into their protoplasm solid particles of various kinds. The cells which are known to possess phagocytic properties are the leucocytes, mucous corpuscles, connective-tissue cells, endothelia of blood-vessels and lymphatic vessels, alveolar epithelium of the lungs, and the cells of the spleen, bone, marrow, and lymphatic glands. Metschnikoff studied first phagocytosis in the tail of the tadpole, and found that the separation of this organ at the time this animal is developed into a frog is accomplished by leucocytes. At a time when the hind legs begin to bud the leucocytes migrate into the tail, and at the point where separation is to take place they attack the tissues, minute fragments of which may be seen in the interior of their protoplasm. In the daphnia, the common water-flea, he studied the destruction of a fungus with which these insects are prone to be infected,—by the mikrophagi. When phagocytosis proved successful he witnessed the destruction of the fungus in the interior of leucocytes; on the other hand, when the fungi were present in such large numbers that the leucocytes were unable to destroy or digest them, the daphnia died. Next, he investigated phagocytosis in a number of diseases,—erysipelas, anthrax, relapsing fever, and tuberculosis. In erysipelas the cocci are first attacked by the leucocytes filling the lymph-spaces, and, later, by the fixed connective-tissue cells. In the path of destruction he saw leucocytes loaded with cocci, the latter showing various stages of dissolution. The connective-tissue cells were also engaged in the removal of disintegrated leucocytes. In fatal cases of erysipelas the streptococci multiplied with such great rapidity that the phagocytes were unable to cope successfully with the disease. Ribbert experimented with the spores of aspergillus and mucor, and the results were such that he claimed that spores in the interior of leucocytes, the connective tissue of the liver, and the giant cells which develop in the liver and in the lungs are destroyed, but that their destruction is not owing so much to phagocytic action of the cells as to the exclusion from them of nourishment for the spores, particularly of oxygen. Laer injected into the lungs through the trachea cultures of the staphylococcus in rabbits, with the result of causing a catarrhal inflammation. The cocci were removed by leucocytes and the embryonal epithelia of the alveoli. During the first week these cells contained many cocci, but during the second week they disappeared in the cells, and the animals recovered.

Metschnikoff's doctrine of phagocytosis has met with violent opposition by a number of eminent pathologists, and foremost among them we find Baumgarten. In a number of publications, this author has taken a positive and firm stand against the claim that cells have the power to digest or destroy the microbes which inhabit their protoplasm. Holmfeld, Bitter, Prudden, and Nuttal have also arrayed themselves against Metschnikoff. With some modifications Klebs is a believer in phagocytosis. In a very interesting paper on this subject, Osler gives the result of his own observations on the phagocytic action of the cells lining the bronchial tubes and the alveoli of the lungs. He shows very conclusively how minute foreign particles are eliminated by means of the phagocytic action of the cells. In connection with the subject of inflammation, the doctrine of phagocytosis should be employed in a wider sense than was assigned to it by Metschnikoff. In the first place, the accumulation of leucocytes at the seat of inflammation must be considered in the light of a mechanical barrier, an attempt to protect the tissues against infection. Unfortunately, in acute inflammation, this wall is usually more apparent than real, as the microbes become diffused through the plasma-stream, and are transported by the leucocytes themselves; hence the progressive nature of the process. The connective-tissue proliferation proves more successful than emigration in limiting the dissemination of micro-organisms in the tissues, as the new cells, as long as they remain attached to the matrix which produces them, remain stationary, and mechanically block the avenues through which dissemination takes place. It is the impermeable wall of granulation tissue which surrounds a suppurating depot, which finally limits suppurative inflammation. In the next place, the phagocytes are scavengers which remove foreign dead particles from the tissues. Langhans was the first to show that extravasated blood did not simply disintegrate and disappear, but that the connective-tissue elements were actively at work, and that many of the colored corpuscles disappear in their interior. Rosenberger implanted stained aseptic tissue into the abdominal cavity of animals, and, on examining the parts a few weeks later, found that not only had the tissues been completely removed by leucocytes, but he was able to follow the course of the leucocytes, after they had left the feeding-ground, by colored lines, all of which were seen to radiate from the place where the stained tissue had been fixed. In different pathological conditions where tissue proliferation was in process, Klebs could find positive evidence that wandering cells which had undergone fragmentation had been appropriated by the embryonal cells as food, as fragments of the nuclear chromatin of the leucocytes could be discovered in the protoplasm of the new cells. In the reparative process which follows the subsidence of inflammation, a great deal of cellular *débris* is to be removed, and this work is performed by the phagocytes, notably by the fixed tissue-cells in a state of proliferation. The vegetative capacity of the cells is augmented by the reception into their protoplasm of nutritive material furnished them by cells which have succumbed in the struggle. Metschnikoff believed that the destruction of micro-organisms in the interior of phagocytes was an active process, and that the protoplasm had a sort of a digestive action upon them. To prove the correctness of this supposition, he made some experiments with the bacillus of tuberculosis. He injected a pure culture of the bacilli into the subcutaneous tissue of white rats, and, later, produced artificially suppuration at the seat of injection. Two months later he found bacilli in the pus-corpuscles in an unchanged condition, and without having lost their power of reproduction. As in other experiments he had witnessed the destruction and disappearance of the same bacillus in living cells, he concluded that phagocytosis is an active process which can only take place in a living cell, and is suspended with the death of the cell. There are few at this time who regard the destruction and disappearance of microbes in phagocytes as an act of digestion. If, however, microbes in the interior of phagocytes are rendered harmless, or disintegrate and disappear, this fact is an important one, and it is immaterial in what way this result is obtained, whether the microbes are digested by the protoplasm, or whether some chemical substance in the cell-body exerts an inhibitory effect upon them, or, finally, whether for want of a proper nutrient material they are starved, as it were. The results of experimental research have furnished positive evidence that infective processes terminate most favorably where the conditions described as phagocytosis are accomplished most satisfactorily.

When the struggle between a microbe and a phagocyte turns out in favor of the latter, the microbe does not multiply in the protoplasm, or ceases to do so before the protoplasm is destroyed, and, as the microbe cannot leave without dissolution of the cell, it remains within its narrow confinement and is destroyed, either by some as yet unknown chemical substance or dies from starvation; in either event the vitality of the cell is not impaired, and the microbe disintegrates and disappears. (Fig. 42, A.) If the conditions for the growth and development of the microbe in the protoplasm of the cell are more favorable, intra-cellular multiplication of the microbe takes place, the ptomaines which are eliminated produce coagulation necrosis in the protoplasm, the cell disintegrates, and the intra-cellular culture is liberated in an active condition (Fig. 42, B). In cases of unsuccessful warfare of the phagocytes against invading micro-organisms, the mechanical obstruction composed of emigration corpuscles and embryonal cells is broken down, and the rapid increase of micro-organisms at the seat of inflammation gives rise to extensive local and often general infection. From a practical standpoint it can be said that all therapeutic measures which influence favorably the process of phagocytosis, in the broadest meaning of this word, are calculated to exert a potent influence in arresting or limiting infective processes.

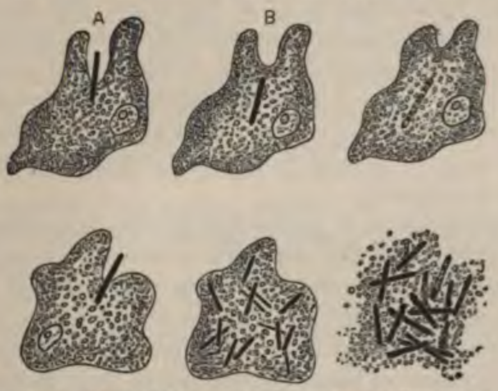

FIG. 42.—PHAGOCYTOSIS. STRUGGLE BETWEEN ANTHRAX BACILLUS AND LEUCOCYTE. A, successful phagocytosis; B, unsuccessful phagocytosis.

CHRONIC INFLAMMATION.

Chronic inflammation differs from the acute form only in degree. The vascular changes which have been described come on slowly, and are never as marked as in acute inflammation, and on this account the emigration of blood-corpuscles occurs slowly, and in some instances it is entirely wanting. The inflammatory product is largely, and in some cases exclusively, composed of embryonal cells derived from fixed tissue-cells. The *noxæ* which excite chronic inflammation are such that exert their deleterious effect more on the tissue-cells directly than the capillary vessels. Their primary action on the tissues consists in increasing the vegetative capacity of the cells; hence, mature cells are transformed into embryonal or granulation tissue and remain in this condition as long as the *noxæ* exist, and retain their pathogenic qualities or otherwise until the new cells undergo retrograde metamorphosis. If in a chronic inflammation degeneration of the embryonal cells has not taken place, and the primary cause has ceased to act, the new tissue is either removed by absorption or is converted into mature tissue, in which event the inflammation has resulted in hyperplasia. Syphilitic gummata, which are composed almost exclusively of embryonal tissue, disappear promptly under a vigorous antisyphilitic treatment, because by such treatment the micro-organisms which have caused the lesion are either destroyed or at least have been deprived for the time being of their pathogenic properties.

Chronic inflammation is represented by that large class of affections which are included under the name *granulomata*. These swellings, irrespective of their primary microbic cause, are composed of what is known as granulation tissue. Some pathologists have been inclined to classify them with tumors, because their development is seldom attended by well-marked symptoms of inflammation, and in their methods of regional and general dissemination they bear a close resemblance to the malignant tumors. Their obstinacy to successful treatment does not depend upon any malignant qualities of the tissues of which they are composed, but upon the difficulty of eliminating or rendering inert the primary cause by internal medication or operative procedures.

All granulomata are inflammatory in their origin, and under the microscope present all the characteristic appearances of inflammation. Histologically they are composed of embryonal cells which correspond to the type of the tissues in which or from which they have developed. In a tubercular nodule we find giant cells, epithelioid cells, the ordinary granulation cell, and leucocytes. Actinomycotic swellings are composed almost exclusively of embryonal connective tissue. Many of the granulomata contain Ehrlich's plasma-cells (Mastzellen), of unknown origin, composed of a finely-granular mass around a vesicular nucleus. On staining with aniline colors, the nucleus remains unchanged, while the granules are deeply stained. The cells are about the size of a leucocyte, either spherical or somewhat elongated in shape. In some cases the outer portion of the inflammatory product, being sufficiently remote from the infected area, is converted into a firm connective-tissue capsule, which limits the extension of infection, while in its interior, from the presence of the specific micro-organisms, but probably more on account of inadequate blood-supply the tissues undergo rapid retrograde degenerative changes.

Secondary infection in a granuloma, either through the circulation, or, what is more common, from without, through some minute infection-atrium, is a not uncommon occurrence. Secondary infection almost always means localization of pus-microbes in the granulation tissue and a breaking down of the latter into pus-corpuscles. The serious consequences which follow suppurative inflammation of a gumma developing after incision made upon a wrong diagnosis is well known. Infection of a large tubercular depot with pus-microbes after incision without proper antiseptic precautions, or after spontaneous evacuation, is followed by destruction of the remaining granulations, profuse suppuration, and not infrequently by death from sepsis. Actinomycosis gives rise to a large granuloma without any tendency to suppuration until infection takes place with pus-microbes, when the granulations melt away rapidly, leaving a deep ulcer with ragged, undermined margins, and a speedy extension of the combined infective processes following in its course the connective tissue.

The secondary infection, however, may prove beneficial and become the means of complete elimination of the products and micro-organisms of the primary infection. In this way a localized tubercular lesion is sometimes cured spontaneously by suppuration. A suppurative inflammation of a tuberculous gland of the neck is often followed by complete removal of the bacilli-containing tissues and a permanent cure. All chronic inflammatory processes are attended by recurring attacks of acute exacerbations. If during these attacks in the periphery of the chronically-inflamed area a more active cell proliferation is initiated, the conditions for a more successful phagocytosis are improved and the acute attack has proved a curative measure.

The surgeon often resorts to measures which result in the transformation of chronic into an acute inflammation, in imitation of nature's efforts in the same direction. In illustration of this, I will only mention ignipuncture. The fenestration of a chronic inflammatory swelling under strict antiseptic precautions has proved a valuable therapeutic measure by securing drainage, but more especially because around each tubular eschar made with the needle-point of a Paquelin cautery a zone of active tissue proliferation is created, and the new tissue, by undergoing transformation into cicatricial tissue, serves a useful purpose in starving out microbes that have escaped the cautery. Another instructive instance of the benefits which accrue from the substitution of an acute for a chronic inflammation is found in the use of jequirity in ophthalmic practice. The powdered bean or some other preparation of this drug, when brought in contact with the conjunctiva, produces a violent inflammation which has frequently proved a curative measure in the treatment of trachoma and some forms of pannus of the cornea.

One of the ways in which an acute inflammation acts beneficially in promoting the process of resolution in tissues the seat of a chronic inflammation is by its stimulating action on the capillary vessels. The active hyperæmia may become the means of clearing partially-obstructed capillary vessels of implanted colorless corpuscles, and thus remove from the weakened tissues not only the mechanical causes which have maintained the chronic congestion, but also the intra-vascular cause of the inflammation—the microbes. When the infected corpuscles reach the general circulation there is a chance for more effective phagocytosis and elimination of the microbes through one or more of the excretory organs.

SYMPTOMS AND DIAGNOSIS OF INFLAMMATION.

For practical purposes, inflammation may be divided into acute, subacute, and chronic, according to the intensity of symptoms and the time required to reach one of its terminations. The nature of the primary cause determines the course and nature of the inflammation. The microbes of suppuration, erysipelas, anthrax, glanders, tetanus, and gonorrhœa cause acute affections, while the micro-organisms of tuberculosis, lepra, and actinomycosis cause lesions which are noted for their chronicity. Acute inflammation may become subacute and finally chronic, as in suppurative osteomyelitis, where, if the disease is multiple, in the first bone affected it pursues a very acute course; while often in the successive bones attacked it is less intense, and not infrequently in the last bone involved it appears as a chronic affection. A chronic inflammation may be followed by a subacute or acute attack, as is frequently observed in tuberculosis complicated by secondary infection with pus-microbes. In acute inflammation the local and general symptoms are so well marked that no difficulties are in the way of recognizing its existence, and it only remains to decide upon its character. The fever which attends the inflammation is only a symptom, and indicates the introduction into the general circulation of phlogistic substances from the products of exudation or the fixed tissue-cells which have undergone pathological changes. Microbes that cause acute inflammation differ greatly as to the amount or intensity of action of the phlogistic substances which they produce in the inflamed tissues affected; also exert an important influence in modifying the febrile disturbance. Suppuration caused by the micrococcus pyogenes tenuis is not attended by so high a temperature as when produced by the staphylococcus or streptococcus. The rise in temperature which accompanies inflammation is due either to the introduction into the circulation of fibrin ferment resulting from the destruction of leucocytes or the production of ptomaines by the specific action of microbes on the tissues, which act as phlogistic substances when introduced into the general circulation,—a fact which has been abundantly demonstrated by clinical observation and experimental research. As soon as the causes which have produced the rise in temperature in inflammation have been rendered inert by phagocytosis, or have been eliminated with the removal of the inflammatory product, the fever subsides. The general disturbances, such as headache, vomiting, loss of appetite, thirst, and the ever-present feeling of lassitude which attends acute inflammation of all kinds, are caused by the fever and the presence of toxic substances in the blood. The symptoms of inflammation, which have been described at length, must be studied separately and conjointly in each form of inflammation, and their individual and mutual significance carefully estimated. A local rise in temperature is of more diagnostic value in ascertaining the existence of inflammation than fever, as the latter can be caused by the absorption of fibrin ferment from any causes which destroy the colorless blood-corpuscles and the absorption of the products of tissue disintegration in malignant tumors; while a permanent increase of the temperature at the seat of the disease denotes almost infallibly the existence of inflammation. In reference to the extension of the inflammatory process, it can be said that this will be influenced by the anatomical structure of the part involved and the manner of diffusion of the microbe which causes the inflammation. If a mucous or serous surface is affected, infection is prone to spread rapidly by continuity of tissue and the mechanical dissemination of the microbes on the surface in the mucous secretion, and by the movements of one serous surface upon the other. In erysipelas the inflammation spreads rapidly, as the microbe is diffused through the lymphatics and connective-tissue spaces. In phlegmonous inflammation the pus-microbes find no mechanical barriers, and are rapidly distributed over a larger area through the connective-tissue spaces. The same manner of diffusion is observed in anthrax if the bacillus finds ingress into a part supplied with an abundance of loose cellular tissue, while the disease remains circumscribed and presents itself in an indurated form if it is located in tissues which do not present such favorable anatomical conditions for extension of the local invasion. The nature of the inflammatory product always answers to the specific action of the microbe as the tissues which caused the inflammation. Thus, an inflammation caused by pus-microbes will result in the formation of pus; while the microbes which produce chronic inflammation, as a rule, only convert the pre-existing mature into embryonal tissue. The microbes which have a short existence in the tissues may give rise only to intense hyperæmia and a moderate emigration of the colored blood-corpuscles, as, for instance, the streptococcus of erysipelas. The genuine, uncomplicated erysipelatous inflammation is of such short duration that perfect restoration of the parts is accomplished in a few days.

PROGNOSIS.

The most favorable termination of inflammation is resolution, with *restitutio ad integrum* of structure and function of the tissues which were the seat of the inflammatory process. Resolution is only possible if the emigration of blood-corpuscles is moderate in quantity and none of the cellular elements of the exudate are transformed into pus-corpuscles. If exudation take place rapidly, the connective-tissue spaces are completely blocked with the emigration corpuscles and the products of coagulation necrosis, which seriously impairs or completely arrests plasma circulation, and, by pressure upon the blood-vessels, may interfere with the capillary circulation to such an extent as to cause necrosis. Resolution, as has been previously stated, signifies that, after subsidence of the symptoms of inflammation, the part is left in a condition capable of removing the inflammatory product and of repairing the damage done. Many of the leucocytes which have retained their vitality immigrate back into the general circulation either through the walls of capillaries or, what is more frequent, through the lymphatic system. The remaining leucocytes and colored corpuscles undergo degeneration and are removed by absorption. Fibrin which has formed in the tissues is transformed into a granular mass, and is removed in a similar manner. Embryonal cells which have become detached, or have been damaged by the inflammation, are also removed by absorption after they have undergone granular degeneration. The transudation is removed by absorption as soon as capillary circulation is restored and the connective-tissue spaces have been cleared of their cellular contents. The capillary wall is repaired, and any tissue defects are restored by proliferation of the fixed tissue-cells. The inflammatory exudate may prove a source of danger when, by its mechanical pressure, it interferes with the function of important organs, as the brain, heart, or lungs. A moderate transudation within the skull from inflammation of any of the meninges can produce death from compression of the brain; a pericardial effusion, when sufficient in amount to interfere mechanically with the action of the heart, causes death by syncope; and a copious effusion into the pleural cavity, especially if it come on rapidly, may impair respiration to such an extent as to result in death from apnœa. A slight croupous exudation upon the vocal cords or œdema about the entrance to the larynx destroys life by preventing, in a purely mechanical way, the entrance into the lungs of an adequate quantity of air. Inflammation is greatly modified by the age and general condition of the patient. Infants and persons advanced in years possess little power of resistance, and, when attacked by inflammation, the disease is prone to become diffuse and lead to serious pathological changes. The same can be said of persons who have been debilitated by antecedent diseases or intemperate habits. The greatest danger in the different forms of inflammation, as far as life is concerned, consists in the introduction into the general circulation of septic material produced in the inflamed part by the action of microbes on the tissues. This general infection, occurring in the course of a localized inflammation, appears either as a symptomatic fever, which disappears with the subsidence of the local process, or as a progressive septicæmia, pyæmia, or septico-pyæmia. The latter diseases will be considered in separate chapters. Tubercular affections are always attended by the danger incident to extension of the process to other organs by dissemination of bacilli through the lymphatic channels or blood-vessels. Chronic suppuration finally causes amyloid degeneration of important organs, and death ensues from this cause. In summing up what has been said under this head, it is evident that the prognosis rests mainly upon the intrinsic pathogenic qualities of the microbe which has caused the inflammation; the anatomical structure, location, and physiological importance of the part or organ inflamed; the general condition of the patient, and the accessibility to and feasibility of treating the disease by direct radical surgical means.

TREATMENT.

As inflammation *per se* is no disease, but an effort on the part of the organism and the tissues affected to eliminate or render harmless the primary cause, the treatment must be, in each individual case, purely symptomatic. A proper appreciation of the nature and tendencies of inflammation is an essential prerequisite to rational treatment. In surgery the prophylactic treatment of inflammation is the most important and satisfactory. The prevention of inflammation in accidental and operation wounds by strict antiseptic precautions has made modern surgery what it is. The surgeon has it now in his power, by resorting to antiseptic measures, to prevent the innumerable and formerly too often fatal wound complications. Lister has inaugurated a new era in surgery, and his work, as well as that of his early enthusiastic followers, has been the means of saving annually thousands of lives. The mortality of even the most desperate operations where the antiseptic treatment can be followed to perfection has been so much reduced that operative surgery has received a new impetus, and operations are devised and put in practice almost daily which formerly would have been looked upon as a freak of imagination or the outcome of a diseased brain. The prophylactic treatment of inflammation in dealing with wounds, or other avenues through which infection can take place, consists of securing for the place deprived of the effective protection against the entrance of pathogenic micro-organisms—the intact skin or mucous membrane—an aseptic condition by antiseptic measures, and to bring in contact with it only things that have been thoroughly sterilized.

In inflammation without an external tangible infection-atrium we must take it for granted that microbes have entered the circulation through slight defects, the existence of which, perhaps, the patient does not remember, and which have left no appreciable marks of their former existence, or infection has taken place through some of the appendages of the skin, or through a mucous membrane, with localization of the microbes in a part or organ previously prepared for their reception and growth; that is, in a location presenting a *locus minoris resistentiæ.*

Recognizing the fact that inflammation, wherever it occurs, is produced by the action upon the vessel-wall and the tissues outside of it of specific micro-organisms, it would appear that the most rational indication for treatment would be to resort to such means which would destroy the microbes in the tissues as soon as their presence is manifested by their action. This would imply the saturation of the inflamed tissues with germicidal solutions, which from laboratory experiments are known to be effective in destroying such microbes; hence, it has been advised to resort to

Parenchymatous Injections.—This method of treatment was strongly advised and extensively practiced by Heuter long before the direct relationship between certain microbes and definite forms of inflammation had been demonstrated. Heuter claimed that every inflammation was caused by certain *noxæ* introduced from without, and which he aimed to destroy by saturating the inflamed tissues with an antiseptic solution. His favorite remedy was a 3- to 5-per-cent. solution of carbolic acid. The instrument which he used was an ordinary Pravaz syringe, with a long needle provided with a number of small lateral openings. In adults he injected as much as 10 grammes at a time of a 3-per-cent. solution. In using this method in the treatment of large, granulating, tubercular foci he employed what he termed an *infusor*, composed of a graduated glass cylinder, joined with the needle by means of a rubber tube. By this method of injection the fluid diffused itself through the soft, granular mass by its own weight. In the treatment of tubercular lesions Heuter claimed for the parenchymatous injections of carbolic acid great curative powers. Rational as this method of treatment appears, it has not yielded the results that were anticipated. The living tissues cannot be compared with a test-tube. Nitrate of silver, iodine, permanganate of potassa, corrosive sublimate, and other potent germicidal agents have been used since, but the results, on the whole, have been anything but satisfactory. If this method of treatment is to be successful in the treatment of acute inflammation, it must be instituted at an early stage, at a time when only a limited area of tissue has been infected, as, under such circumstances, if the area of infection could be accurately outlined, it would be possible to saturate the tissues with an antiseptic solution without running the risk of killing the patient by administering a toxic dose of the drug employed, which might be the case if a larger area were treated in a similar manner. If we remember that the microbes are diffused throughout the entire exudation, and constitute the most important element of the inflammatory product, it is easy to understand that sterilization of the inflamed tissues by means of parenchymatous injections is not an easy task, and we are then in a position to realize why this method of treatment has not proved more uniformly successful. Most of the germicidal agents heretofore employed in this manner, when brought in contact with the tissues, form compounds which prevent further diffusion, and therefore each needle-puncture sterilizes only a very small portion of the inflamed district. It is possible that in the future non-toxic, but at the same time effective germicidal, substances will be discovered which can be used in larger quantities, and in this event the treatment of inflammation by parenchymatous injections will have a wide range of application, and will be practiced with better success. At present this method has a limited field of application in the treatment of the various forms of inflammation. Under no circumstances should the amount of the drug used exceed the dose which it would be safe to administer internally, and the danger of a poisonous dose should be remembered in repeating the injection. An ordinary hypodermic syringe with a long needle can be used in making the injection. That the needle and syringe should be perfectly aseptic is to be understood as a matter of course, as unclean instruments have often been the means of conveying a fatal disease. Multiple punctures are to be preferred, as in this manner, by using the same amount of fluid, more tissue can be saturated than by a single puncture. Before making the punctures the surface must be disinfected. The object should be to bring the antiseptic solution in contact with as much of the injected tissues as possible, and if the disease show a tendency to spread it is advisable to go beyond the zone of infection, as, for instance, in cases of erysipelas and anthrax. Many accessible tubercular affections are greatly benefited by parenchymatous injections of carbolic acid. Recently, intra-articular and parenchymatous injections of iodoform have been strongly recommended in the treatment of articular and other forms of surgical tuberculosis.

Antiphlogistic Treatment.—An erroneous conception of the nature and tendencies of inflammation has for centuries induced the ablest teachers and practitioners to advocate and practice what they termed the antiphlogistic treatment of inflammation. This included blood-letting, cupping, leeching, and the internal use of emetics and cathartics. It was urged that as inflammation was attended by an increase of heat, swelling, and redness, such remedies should be employed as will reduce arterial tension. Venesection is now seldom, if ever, resorted to in the treatment of any form of inflammation. An unimpaired *vis a tergo* is one of the best means to prevent stasis within the inflamed capillaries, and practical experience has shown that all remedies and agents which diminish the intra-arterial tension only diminish the prospects for a favorable termination of the inflammation. Cohnheim showed experimentally that the threatened stasis in the exposed mesentery of the frog was avoided by injecting into one of the veins 1 centimetre of a 6-per-cent. solution of sodic chloride. If, under similar conditions, a considerable quantity of blood is abstracted, the congestion can be seen to terminate in a short time in complete stasis. While venesection in the treatment of inflammation has been discarded, the direct abstraction of blood from the inflamed part hss proved a useful therapeutic resource. Genzmer showed that in the inflamed mucous membrane of a frog scarification hastened resolution. In order to be of benefit the scarification must be made through the inflamed part, so as to unload directly the dilated and engorged capillary vessels, and on this account this method of treatment is only applicable when the inflammation is superficial and affects accessible parts. Leeches should never be used, as infection from this source has frequently resulted disastrously. The scarification used for cupping is difficult to keep aseptic, and the number and depth of the scarifications to be made are not under the control of the surgeon, and for these reasons this instrument has only an historical interest and antiquarian value. The scarification should be made with a sharp scalpel, and the bleeding encouraged by applying warm water. Scarification is followed by great relief in inflammation of accessible mucous membranes, and has recently been very strongly recommended in the treatment of erysipelas for the purpose of preventing the extension of this disease.

In the different forms of septic inflammation attended by severe general symptoms the gastro-intestinal canal often participates in the process, and vomiting and diarrhœa become conspicuous and often distressing symptoms. These symptoms should not be checked, as they indicate an attempt on the part of the organism to eliminate through the gastro-intestinal mucous membrane microbes and ptomaines which have reached it through the general circulation. The surgeon should assist this effort by administering a few doses of calomel, followed by a saline cathartic, which will often control the vomiting and diarrhœa more promptly by removing the cause than medicines employed to arrest the process of elimination.

Physiological Rest.—One of the most urgent indications in the treatment of inflammation is to secure for the part affected a condition approaching physiological rest. In ulcerative affections of the gastro-intestinal canal the patient should abstain from taking food by the stomach. Fixation of the chest by means of broad strips of adhesive plaster affords great relief in pleuritis. An inflamed point must be immobilized by some kind of a splint. A chronic cystitis usually yields to supra-pubic or perineal drainage of the bladder after all other measures have failed. In inflammatory affections of the eye exclusion of light is one of the most essential features of successful treatment. Patients suffering from inflammatory affections of the tonsils, pharynx, and larynx should use their voice as little as possible. In cases of acute inflammation of the brain or its envelopes the patients must be kept in a dark room, and absolute quietude enforced.

Elevation of Inflamed Part.—From the diminished *vis a tergo* on the distal side of the capillary vessels, venous engorgement is as pronounced as increased arterial tension on the proximal side of the inflamed capillary vessels, and elevation of the inflamed part improves the vascular disturbances by the force of gravitation favoring the return of venous blood. The importance of elevation of the inflamed part becomes manifest in the treatment of inflammatory affections of the extremities. In phlegmonous inflammation of the hands or feet the throbbing pain is always aggravated if the limb is kept in a dependent position, and promptly relieved upon placing it in an elevated position. Elevation not only alleviates the pain, but is at the same time the most effective means of removing the œdematous swelling. If necessary elevation can be combined with suspension in order to secure more perfect rest for the inflamed part. In severe acute inflammation it is not only necessary to secure rest for the part inflamed, but of the whole body, and in such cases the patient must observe the recumbent position in bed, as all muscular movements and all unnecessary strain upon the blood-vessels cannot but be productive of harm by favoring the ingress into the circulation of micro-organisms and their ptomaines from the seat of inflammation, or, perhaps, result in embolism from detachment of a portion of a thrombus,—an accident which possibly might not have occurred otherwise.

Application of Cold.—Cold has been resorted to indiscriminately and empirically in the treatment of inflammation. Cold is a potent agent for good or harm, according to the stage of inflammation during which it is applied. The sensation of heat, both subjective and objective, naturally suggested the use of this remedy. The application of cold is of great benefit during the earliest stage of inflammation, at a time when exudation is only beginning and the capillary vessels are dilated and only partially obstructed. Cold, when applied under these circumstances, becomes a valuable remedial agent (1) by producing contraction of the small blood-vessels; (2) by producing at least an inhibitory effect upon the micro-organisms in the inflamed tissues. The contraction of blood-vessels which takes place under the application of cold has a tendency to clear the capillaries of their contents and to prevent further mural implantation. Micro-organisms can only multiply at a certain temperature, and if this can be kept at a point low enough to prevent their increase in the tissues by the application of cold this agent fulfills one of the causal indications in the treatment of inflammation. If, however, stasis has already taken place in the capillaries first affected the application of cold will prove harmful, as it will tend to prevent the formation of an adequate collateral circulation. Cold acts most beneficially when the inflammation is located in the superficial parts, but its prolonged use will reach even deep-seated structures, as the pleura, peritoneum, the brain and its envelopes, the joints and bones. When it appears desirable to resort to the use of cold, this remedy should be applied in the form of an ice-bag. The part to which the ice-bag is to be applied can be covered with several layers of a wet towel, as otherwise the prolonged use of the direct application of ice may freeze the skin. The sensations of the patient can actually be taken as a safe guide as to the length of time it should be continued.

Antiseptic Fomentations.—The ordinary filthy poultice of flaxseed, slippery elm, bread and milk, has no longer a place among the resources of the aseptic surgeon. The common poultice is a hot-bed for bacteria, and, as such, it should be discarded. In the treatment of an ordinary furuncle with poultices, I am sure that almost every surgeon must have seen occasionally the development of innumerable minute daughter-furuncles in the surface covered by the poultice. In phlegmonous inflammation of the fingers or hand the prolonged use of the poultice is followed by maceration of the skin, extensive œdema of the superficial structures, a flabby condition of the granulation,—in fact, all the evidences which point to the poultice as a means of favoring the extension of the infective process. When inflammation has passed beyond the stage where cold exercises a favorable influence, or where cold applications increase the suffering, warm antiseptic fomentations should be employed. The surface to which they are to be applied should be thoroughly cleansed with warm water and potash soap. The antiseptic solution to be used should be selected according to the age of the patient, or the area affected, with a special view of guarding against the absorption of a toxic dose of the drug employed. Acetate of aluminum, in the strength of 1 per cent. dissolved in sterilized water, is a safe preparation under all circumstances. Boracic and salicylic acid are efficient and safe preparations. Greater care is necessary in the use of carbolic acid and corrosive sublimate, as, when concentrated solutions of these drugs are used for any length of time in infants, the aged, or persons suffering from organic disease of the kidneys, there is danger of poisoning from absorption through the intact skin. In children and marantic persons it is safer to use acetate of aluminum, salicylic or boracic acid, and reserve the more potent antiseptics for adults suffering from circumscribed inflammatory lesions. Hot fomentations act as derivatives and favor the formation of collateral circulation; at the same time they relieve pain. A number of layers of hygroscopic gauze or flannel cloth are wrung out of one of these antiseptic solutions and applied over the affected part, and for the purpose of retaining the heat and of preventing evaporation of the solution the compress is to be covered either with gutta-percha, rubber sheeting, or macintosh cloth, and the dressing is retained by an appropriate bandage. The compress is removed two or three times a day, again wrung out of the hot solution, and re-applied as before. Absorption through the skin of the antiseptic substance used may have a direct influence in diminishing the intensity of the cause which produced the inflammation, and prepares, in an admirable manner, the field for any operation which may become necessary in the future.

Antipyretics.—If the rise in temperature which attends many of the acute inflammatory affections is due to the introduction into the circulation of phlogistic substances which are produced by the action of the micro-organisms in the inflamed tissues, it is not difficult to conceive that its artificial reduction by the internal use of chemical substances is not followed by any permanent benefit. The rational treatment of the fever consists of such local measures as will remove its cause. Antifebrin, antipyrin, salicylated soda, quinine, and other antipyretic drugs, when employed in large doses, will usually reduce the temperature several degrees for a few hours, but this is always accomplished at the expense of the forces which are laboring to clear obstructed paths, and on this account their use has resulted in more harm than good to the patient. Quinine is the least objectionable of the drugs which have been mentioned, and in the beginning of an inflammation, by its known tonic effect on the small blood-vessels, when administered in a large dose, has a favorable effect in preventing rapid dilatation of and stasis within the capillary vessels. If used at all, it should be given in a decided dose,—1 gramme, in solution,—immediately or soon after the development of the first symptoms. Sponging the surface of the body with warm water or the use of warm baths are the most rational antipyretics, as these simple measures do not weaken the heart's action, while they have a decided effect on the temperature, and at the same time add to the comfort of the patient and favor the elimination of microbes through the excretory organs of the skin. As the kidneys are known to eliminate micro-organisms that reach them through the general circulation, their function should be carefully inquired into, and if the secretion of the urine is scanty, diuretics, like liq. ammon. acet., or acetate of potash should be given.

Stimulants.—Just as soon as symptoms of sepsis develop in the course of an inflammation, alcoholic stimulants should be freely administered to meet in time the dangers incident to heart-failure. Stimulants have largely taken the place of antiphlogistics at the present time in the treatment of septic inflammations. Brandy, cognac, or whisky, not in measured doses, but given in quantities large enough to produce the desired effect on the heart, are given at intervals of one or two hours. Champagne is a more diffusible stimulant, and is to be resorted to when the stomach does not tolerate other alcoholics. In chronic cases, Tokayer or Greek sherry are to be preferred. In wasting diseases, a good quality of beer, ale, or porter will do excellent service. In cases where, from any cause, the heart's action is suddenly diminished, camphor or musk can be administered subcutaneously to bridge over the time for the employment of more substantial stimulants.

Diet.—The treatment of inflammation by starvation has been abolished long ago. The strength of the patient must be sustained in time by a nutritious, well-selected diet. Animal broths, beef-tea, and milk should be freely given from the very beginning, and if more substantial food can be digested it should not be withheld. Oysters, eggs, fine-scraped raw meat, or rare roast are excellent articles of food for patients whose strength is being undermined by debilitating, suppurative affections. If the stomach does not retain food, the patient should be nourished by rectal enemata of peptonized milk and beef-tea in quantities not exceeding 4 ounces, given alternately, every eight hours. Ripe oranges and grapes are most always grateful to the patient, and their use should never be prohibited, unless the gastro-intestinal canal is the seat of inflammation.

Tonics and Alteratives.—In protracted inflammatory affections tonic doses of quinine are indicated. Tincture of chloride of iron is an excellent remedy after the acute febrile symptoms have subsided. Under similar circumstances, one or more of the bitter tonics can be given with benefit if the appetite is defective. If there is any history of specific disease, a thorough antisyphilitic treatment will often produce a marked effect for the better on the inflammatory process. Catarrhal inflammation in rheumatic patients is favorably influenced by antirheumatic remedies. Syphilitic lesions are to be treated by potassic iodide and small doses of corrosive sublimate. Tubercular affections call for arseniate of iron, syrup of iodide of iron, and, if the patient's stomach can tolerate it, pure codliver-oil. The latter drug should be given alone, and not in emulsion, in gradually-increasing doses an hour and a half after each meal.

Anodynes.—Remedies to relieve pain must always be used with caution, as in painful chronic affections their prolonged use frequently engender a habit. The cause of pain must be sought for, and, if possible, removed by local measures. In acute inflammation, pain indicates tension in the inflamed part, and prompt relief is obtained by subcutaneous incision. Periostitis and paronychia should be treated by this method. In superficial inflammations scarification answers the same purpose. If opiates are used, a decided dose is better than smaller doses frequently repeated. The anodyne effect of opium is increased by the addition of a minute dose of atropine. Chloral and potassic bromide are to be preferred to opium to relieve the pain of intra-cranial lesions. Phenacetine in ½-gramme doses is a very excellent anodyne in cases of peripheral neuritis. Inhalations of chloroform to allay intense pain should never be resorted to except by the direction of and under the personal supervision of a competent physician.

Massage.—In chronic inflammatory affections systematic massage, scientifically practiced, is an exceedingly important and valuable therapeutic resource. It stimulates the surrounding vessels to increased action, and exerts a potent influence in restoring the normal circulation in the affected capillary vessels, and always promotes absorption. The masseur should be instructed to apply some absorbent preparation before making the manipulations, as the endermic use of absorbent drugs in this manner will increase the efficacy of the treatment. A drachm of potassic iodide or half a drachm of iodoform to an ounce of lanolin will be an excellent preparation for this purpose. Cold and hot douches, passive and active motion, combined with massage, will often expedite a cure.

Counter-Irritation.—Like so many other time-honored methods of treatment, counter-irritation in the treatment of acute inflammation has almost entirely gone out of use. In chronic inflammation, blistering and painting with the tincture of iodine will at least satisfy the patient, if no good result from them; and if he does not recover, he is at least prevented from passing into the hands of charlatans until the time has arrived to resort to more effective and radical measures. Kocher praises the application of the actual cautery in the treatment of chronic tubercular osteomyelitis and synovitis. The seton and moxa have fallen into well-merited disuse for all time to come.

Ignipuncture.—In many chronic affections, where the inflammatory exudation remains stationary for a long time, multiple punctures with the needle-point of a Paquelin cautery, made under strict antiseptic precautions, will have a prompt effect in diminishing the primary cause, as well as in promoting absorption.

CHAPTER V.

PATHOGENIC BACTERIA.

BACTERIA, micro-organisms, microbes, and germs are synonymous terms for certain minute, microscopical, vegetable organisms which. when introduced into the living body, produce the fever and the tissue changes described in the preceding chapter. For a time it was claimed that these minute organisms belonged to the animal kingdom. as some of them were seen to possess spontaneous movements; but now it is generally agreed that they are minute plants, and botanists have made great progress in perfecting a scientific classification. Among the men who have developed this part of botany, the names of Cohn, Zopf, and Nägeli stand pre-eminent.

CLASSIFICATION.

The pathogenic bacteria which will claim our attention belong to the class known as schizomycetes (Spaltpilze). In diameter they vary from 0.001 to 0.004 millimetre, and are composed largely of an albuminoid substance called by Nencki myco-protein. Toward the periphery this substance becomes firmer, and forms a gelatinous envelope, a sort of a membrane, which is said to contain cellulose, and, in some instances, even fatty material. The outer surface of bacteria is frequently covered with a viscid substance, by which many of them are often held together in a mass or group, technically called zoöglœa. Each bacterium represents a cell, although the presence of a nucleus, or something representing such a structure, has not been demonstrated; but its cellular structure is made evident by its intrinsic power of germination or reproduction when surrounded by the necessary conditions for its growth. Some of the bacteria are provided with processes, or cilia, by which, when suspended in a fluid, movements are accomplished; in others motion is entirely dependent on molecular movements described by Brown. Nägeli, and formerly Billroth, claimed that all bacteria had a common botanical source, and that the different forms and actions only represented alteration of form of action of the same plant at different stages of development and under different circumstances,—in other words, that a coccus could be transformed into a bacillus, and *vice versâ;* and that in one instance the same plant caused fermentation, in another putrefaction, and that all infective diseases were caused by the same microbe. Buchner maintained that, by cultivation in different nutrient media, he was able to transform the dangerous bacillus of anthrax into

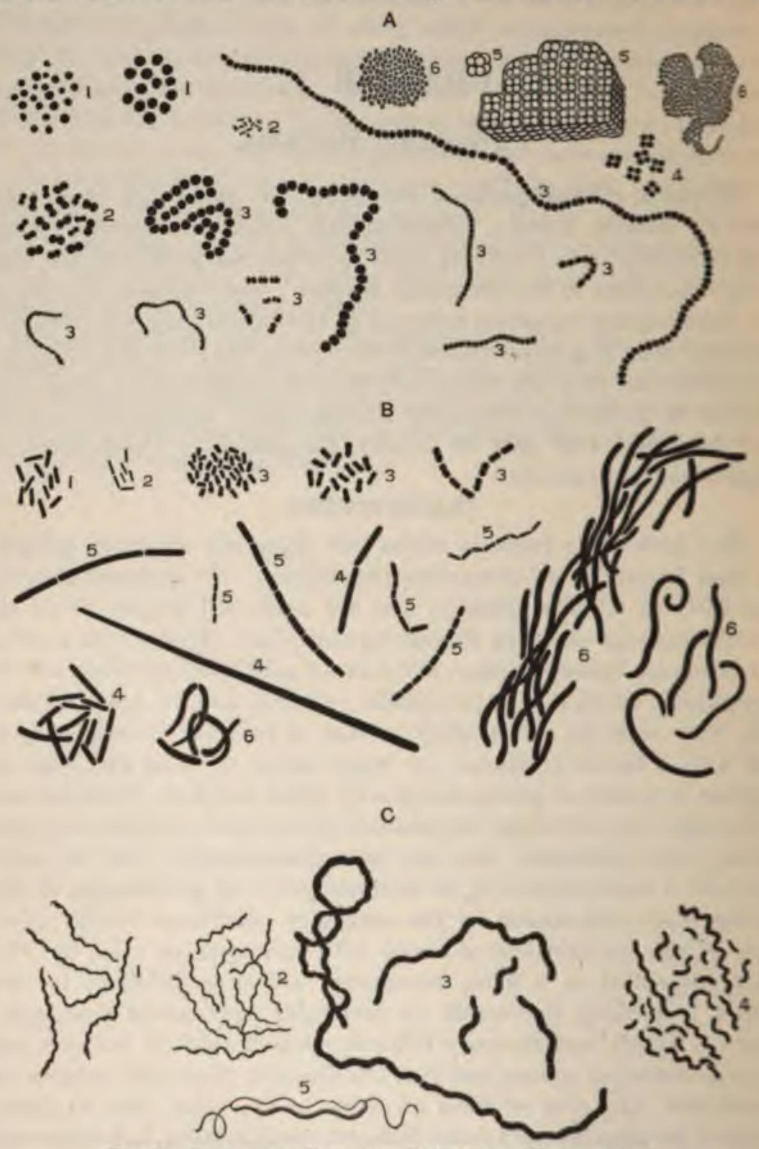

FIG. 43.—DIFFERENT FORMS OF BACTERIA. (*Baumgarten.*)
A, cocci; B, bacilli; C, spirilli.

the harmless bacillus subtilis, and, again, the latter into the former. Cultivation and inoculation experiments on a large scale by most careful observers have shown conclusively that such transformations never take place, and that each microbe not only always retains its shape, but also its specific pathogenic properties. Pus- and other microbes have been cultivated through thirty and more generations without suffering any morphological deviations or losing any of their inherent characteristic pathogenic properties. The three principal forms of bacteria discovered up to the present time, and which have been demonstrated as causes of disease, are: (1) the ball (coccus); (2) rod (bacillus); (3) corkscrew (spirillum). As illustrations for these different forms, de Bary very appropriately takes the billiard-ball, lead-pencil, and corkscrew.

The surgeon has to deal only with the two first forms,—the cocci and bacilli. Modifications of form are frequently met with, as an oblong coccus closely resembles a short bacillus, and a short, broad bacillus with rounded ends approaches the coccus form. Again, a double coccus, or diplococcus, with ill-defined constriction at the point of junction, might, from superficial examination, be mistaken for a bacillus (Fig. 43, A, 2). More than 2 cocci in a row, or a chain of cocci, are called a streptococcus (A, 3). Four cocci arranged in the form of a square are called a micrococcus tetragones (A, 4). Cocci arranged in the form of a bunch of grapes are called streptococci (A, 6). An irregular mass of cocci, when at rest and held together by a viscid substance, is described as a zoöglœa.

MULTIPLICATION OF BACTERIA.

Bacteria multiply with great rapidity in tissues presenting favorable conditions for their growth, or in proper nutrient media kept at a temperature approaching that of the body. Multiplication takes place either by fission or segmentation, by the production of spores, or by both of these methods. The bacillus of anthrax multiplies by fission in the body, by spores outside of the body.

Fission.—The round or globular bacteria,—the cocci,—as far as we know, multiply only by fission. The cell elongates prior to segmentation, when a constriction appears in the centre, which, by becoming deeper and deeper, finally results in complete division of the cell into two equal halves, which soon attain the size of the mother-cell, and, in turn, again undergo the same process. If the new cells remain adherent, and arrange themselves in the form of a chain, a streptococcus is formed. Flügge observed complete division of a coccus in bouillon, kept at a temperature of 35° C., in twenty minutes. If it should require one hour to complete segmentation and for the new cell to attain maturity, a single coccus multiplying by fission, according to Cohn, during one day, would produce sixteen millions of cocci, and at the end of the second day the product would represent two hundred and eighty-one billions in number, and at the end of three days the extraordinary number of forty-seven trillions would be reached. Rod bacteria which reproduce themselves by fission undergo transverse segmentation in the middle, and after complete separation each segment grows to the size of the parent-cell before the process repeats itself.

Spores.—The spores of bacteria represent the seed of flowering plants. Each spore develops into a bacterium, and thus one crop after another is produced, the multiplication increasing with the number of bacteria in the soil. Most of the bacilli multiply by spores. Fructification again takes place, either within the protoplasm of the cell (endospore) or at one or both extremities of the cell (endspore). Fructification is often preceded by a rapid elongation of the bacillus. Multiple endospores usually form in one bacillus simultaneously. The first evidences of the formation of spores within the protoplasm of a bacillus is indicated by the appearance of circumscribed points of cloudiness at equidistant points.

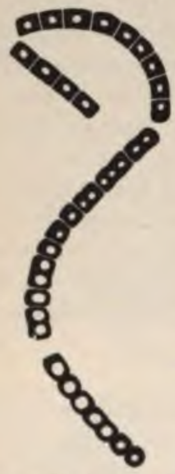

FIG. 44.—ENDOGENOUS SPORE PRODUCTION IN BACILLUS ANTHRACIS CULTIVATED UPON MEAT-INFUSION PEPTONE-GELATIN. × 950. (*Baumgarten.*)

After the expiration of twenty hours the bacillus appears like a string of pearls, each segment of which represents a fully-developed spore. After this the segments separate and each spore develops into a bacillus.

If the bacillus reproduce itself by a single endospore, it does not elongate before fructification, but increases in diameter, especially in the centre, so that it assumes the shape of a spindle; while, equidistant from its ends, changes are observed in the protoplasm which indicate the beginning of spore formation. If the bacillus multiply by terminal fructification, one or both of its ends enlarge, become club-shaped, and the spores pass through the same stages of development as the endospores, and they are liberated in the same manner by liquefaction of the cell-membrane surrounding them. Bacteriologists are familiar with the fact that spores possess a greater power of resistance to germicidal agents than the bacilli which produced them. Mature bacteria are always destroyed by a temperature of 77° C.; most of them succumb when exposed to a heat of 50° to 55° C. On the other hand, some of the spores are known to survive a temperature of 100° to 120° C.

Sternberg has determined the thermal death-point of the following bacteria:—

	Fahr.
Bacillus anthracis (Chaveau),	129.20°
Bacillus-anthracis spores,	212.0°
Bacillus tuberculosis (Schill and Hischer),	212.0°
Staphylococcus albus,	143.6°
Staphylococcus pyogenes aureus,	136.4°
Staphylococcus pyogenes citreus,	143.6°
Streptococcus erysipelatosus,	129.2°
Gonococcus,	140.0°

In all experiments, with the exception of the bacillus of tuberculosis, the microbe was subjected to the specified heat for ten minutes; the tubercle bacillus was destroyed in four minutes. Such resisting spores are often not destroyed by boiling continued for several minutes, and yield only slowly and frequently imperfectly to germicidal chemical agents. Surgeons are aware that such spores may remain dormant in the body for years without giving rise to any symptoms until aroused to activity by surrounding conditions favorable to their growth and development.

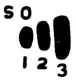

FIG. 45.—SPORE OF BACILLUS OF ANTHRAX. × 6-700. (*De Bary.*)

S, ripe spore before germination; 1, 2, 3, three successive stages of germinating spore; 3, young rod.

CULTIVATION OF BACTERIA.

The first cultivation experiments were made with fluid nutrient substances, such as bouillon, different animal broths, and solutions of sugar. Koch introduced solid nutrient media, which not only serve as food for the bacteria, but at the same time present the great advantage that the colonies can be seen with the naked eye, and their microscopical appearances, as well as the visible action of the bacteria on the nutrient substance, often are sufficient to convey reliable information to enable the observer to form a positive conclusion in reference to the kind of microbes of which the colonies are composed. In fluid nutrient media the bacteria cause turbidity, or they appear as a thin film on the surface; or zoöglœa masses show themselves as swimming flocculi; or, finally, when the fluid has been exhausted of its nutrient supply the spores settle at the bottom of the vessel and appear as a pulvurulent deposit. Upon solid nutrient media each kind of bacteria appear as isolated, distinct colonies, and as such can be recognized by the naked-eye appearances.

The substance used first by Koch as a solid medium, and which is now used more than any other, was gelatin. Later, a jelly-like substance called agar-agar, obtained from several sea-weeds on the coasts of Japan and India, was found superior to gelatin where a higher than ordinary temperature was required to cultivate certain microbes. Edington prefers a gelatin made of Irish moss to agar-agar, as it is more transparent. Some microbes that will not grow upon gelatin vegetate luxuriantly on solid blood-serum. The tubercle bacillus grows equally well upon solid blood-serum and glycerin agar-agar. This latter substance is easily prepared and is made by adding 6 per cent. of pure glycerin to the ordinary agar medium.

The busy practitioner, who has no time to prepare the media used in laboratory work, can do good bacteriological work by using sterilized potato or bread-paste. The potato is the best medium for the cultivation of chromogenous bacteria, or such as secrete a coloring matter, as upon this substance the color is preserved. The potato is scrubbed with a hard brush under a stream of water. It is then left in a solution of corrosive sublimate (1 to 1000) for an hour or so to disinfect its surface. With a knife rendered sterile by passing it through the flame of a Bunsen lamp, a quadrilateral piece is cut from the centre, and is rapidly transferred on the knife to a glass capsule previously sterilized by heat. Capsule and potato are next placed in steam sterilizer, when the simple apparatus is ready for inoculation. Inoculation is done by charging the point of an aseptic needle with the culture, or substance containing the microbes, and after lifting the capsule half up a number of streaks are made with the needle upon the surface of the potato. A potato-paste, made by adding a sufficient quantity of distilled water to the interior portion of boiled potatoes to make a paste, is used in the same manner and answers the same purpose as sterilized raw potato.

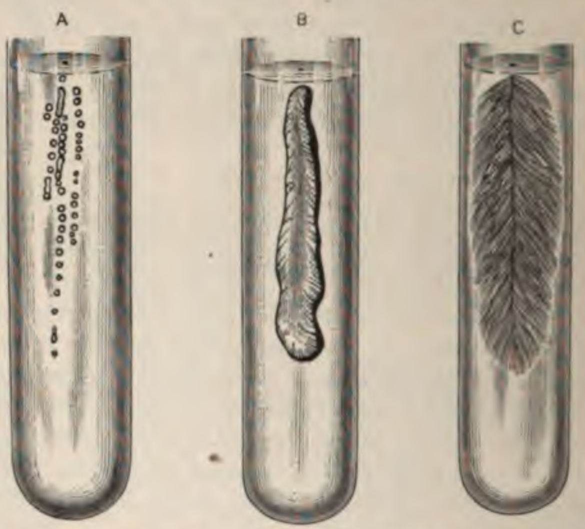

FIG. 46.—GELATIN CULTURES FOLLOWING SURFACE INOCULATION. (*Flügge.*)

Bread-paste is made of stale, coarse bread, thoroughly dried in an oven, but not roasted. It is pulverized in a clean mortar and the powder made into a paste by adding distilled water. The paste is transferred to sterile glass capsules and used in the same manner as potato-paste. If it is employed for the culture of bacteria, it must be neutralized with a solution of carbonate of soda. Some microbes possess the faculty of liquefying the gelatin; others remain as solid cultures upon the surface of the medium, or in its interior. Free access of oxygen to the seat of inoculation is essential for the growth of some microbes, and these were termed by Pasteur *aërobiontic*, while those that germinate with exclusion of oxygen he called *anaërobiontic*. The former class germinate on the surface of the media with or without liquefaction of the soil. If microbes of this kind are inoculated by scratching the surface of the medium with the point of a needle charged with them, the culture appears first at isolated points (Fig. 46, A), which by increase in size become confluent and occupy as a solid mass the whole track made by the needle (B, C).

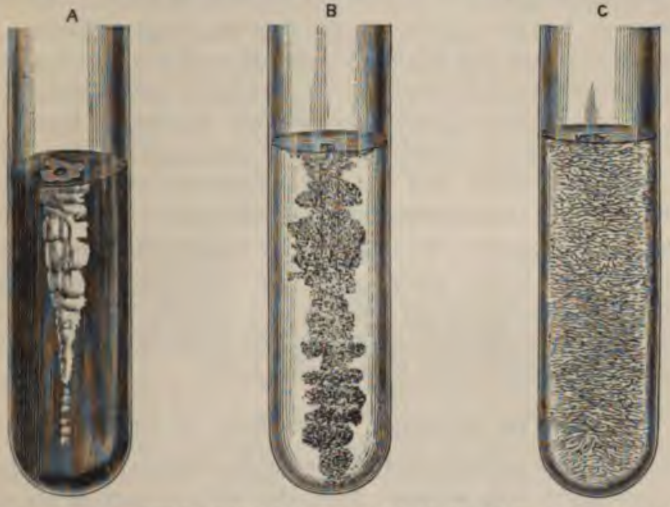

FIG. 47.—CULTURES IN GELATIN GROWING IN THE TRACK MADE BY THE NEEDLE. (*Flügge.*)

In making inoculations with anaërobiontic bacteria the gelatin is punctured with a needle, charged as before, to some depth, and isolated colonies appear in the track made by the needle, which by confluence form a continuous, uninterrupted culture the whole depth of the needle, which increases in diameter by extension in a peripheral direction. Superficial cultures are called streak cultures; deep cultures, stab cultures.

All cultivation experiments must, of course, be conducted under strictest antiseptic precautions, as otherwise there is great danger of contamination of the cultures by the accidental ingress of other microbes, especially of some forms of fungi.

ESSENTIAL CONDITION FOR GROWTH OF BACTERIA.

For the germination of bacteria, besides a proper nutrient substance the other conditions which enable the growth of other plants from seed are necessary, viz., moisture and a certain degree of heat. Inspissation of solid nutrient medium arrests further development of a culture. Bacteria cannot grow upon a perfectly dry medium. Most microbes germinate best at a temperature corresponding to blood-heat, but in this respect the different kinds show great variance, as some vegetate at 10° C., while the growth of others will continue at 65° C. Acids appear to produce an inhibitory effect on the process of germination. Laplace has utilized this fact and advises the addition of citric acid to solutions of corrosive sublimate to intensify its germicidal properties. It is well known that the gastric juice suspends the growth of most bacteria. Bacteria which live on dead substances exclusively are called *saprophytes.* Bacteria which feed on dead substances and can exist in the living tissues only at a certain stage of development are called *facultative parasites*, in comparison with the *obligatory parasites*, which multiply exclusively in the living tissues. As representatives of the former can be enumerated the bacillus of anthrax and cholera, which, under favorable conditions, can multiply outside of the body, while the bacillus of tuberculosis germinates only in the living body.

ACTION OF BACTERIA ON TISSUES OF THE BODY.

The action of pathogenic bacteria on the tissues is a twofold one. In the first place, they abstract from the body a part of its essential constituents; for example, albuminous substances, carbohydrates, oxygen, etc. These substances are not only taken from the fluids of the body, as the blood and lymph, but also directly from the protoplasm of the cells. In the second place, they produce in the body toxic agents from their action on the albuminoid substances. The decomposition of albuminoid substances by the action of bacteria results in the formation of ammonia and its derivatives, the different amines, CO_2, H_2S, indol, scatol, phenol, asparagin, leucin, tyrosine, etc.

Ptomaines.—The common name for the toxic substances of bacterial origin is ptomaines. Brieger has isolated a number of ptomaines from cultures of different bacteria, and Hoffa is now engaged in the same kind of work. Vaughn, of this country, has written a valuable work on this subject, which should be read by all who wish to become familiar with modern surgical pathology. Brieger has isolated a number of toxic alkaloids, cadaverin, neurin, muscarin, and mydalein, which are intensely toxic, while the derivatives of ammonia-dimethylamin, trimethylamin, and triathylamin are much less dangerous substances. The ptomaines, being soluble substances, are readily absorbed, and when introduced into the circulation produce fever and symptoms of sepsis. The ptomaines of the bacillus of tetanus act principally upon the central nervous system, producing characteristic tonic and clonic spasms of definite groups of muscles. The ptomaines also produce a definite local effect,—thus, the ptomaines of pus-microbes transform the leucocytes and embryonal cells into pus-corpuscles, those of the microbe of progressive gangrene destroy the protoplasm of the cell-body directly, while the toxic substances of the microbes of chronic infective diseases transform the fixed tissue-cells into embryonal or granulation cells. Some of the microbes remain in the tissue at the seat of infection; others localize in the lymphatic channels, while, finally, others enter the general circulation and multiply in distant organs. The production of ptomaines usually takes place in the tissues in which localization takes place.

INOCULATION EXPERIMENTS.

The mouse, rat, rabbit, guinea-pig, and dog are the animals usually selected for this purpose. Inoculations are made either with pure cultures, which are injected by means of a sterilized hypodermatic syringe, or infected tissues are implanted under strict antiseptic precautions. Injections of pure cultures are made either into the subcutaneous tissue or one of the large serous cavities, the pleural or peritoneal cavity. The same localities are generally selected for inoculation by means of implantation of infected tissue. For instance, granulation tissue from tubercular lesions is either introduced into a small pocket made in the subcutaneous tissue in the inguinal region of a guinea-pig, or a small fragment is inserted into the pleural or peritoneal cavity through a small incision. Before the incision is made it is absolutely necessary to shave the surface and disinfect it in the usual way. After the implantation is made the wound is closed by suturing with fine catgut, after which it is sealed with collodium. In the course of two or three weeks the subcutaneous graft has become the centre of a local tubercular focus, which soon gives rise to regional infection through the lymphatic vessels, to be followed at the end of five or six weeks by general diffuse miliary tuberculosis. In cases where it is impossible to make a differential diagnosis between a syphilitic and tubercular lesion, inoculation of a guinea-pig with a fragment of the granulation tissue will furnish positive information in the course of a few weeks. If the lesion is syphilitic, the result of the inoculation will be negative; if it is tubercular, local, regional, and general infection will follow in regular order. In making implantation experiments from animal to animal, it is necessary to remove the graft immediately, or soon after death, and to resort to the necessary precautions to prevent contamination during its conveyance from the dead to the living animal. In bacterial diseases which affect the blood, inoculation can be practiced by injecting blood, abstracted from the infected animal, into the subcutaneous tissue or general circulation of a healthy animal, with the effect of reproducing the disease. Anthrax and septicæmia of mice furnish good illustrations of this class of diseases.

ATTENUATION OF PATHOGENIC BACTERIA.

Pasteur opened a wide field for investigation in preventive medicine by his introduction of prophylactic inoculations. He experimented first with the microbe of chicken-cholera and the bacillus of anthrax. The microbe of fowl-cholera was cultivated in chicken-bouillon for three, four, five, or eight months. He found that by this time the virus becomes so attenuated that, when injected into a healthy chicken, it kills only in exceptional cases. Experience showed that attenuation only occurred when the culture is freely exposed to atmospheric air, and therefore Pasteur believed that the prolonged contact of the culture with oxygen diminished its virulence. Chickens inoculated with weak cultures were rendered immune to the action of the active virus. The same author made the discovery that the anthrax bacillus, cultivated in the same way at a temperature ranging between 40° and 43° C., loses its virulence gradually, so that on the ninth day it is rendered harmless. Inoculation with attenuated cultures protected sheep against the active virus. Koch, Gaffky, and Loeffler found that a culture of anthrax bacilli twenty days old, attenuated at a temperature of 42° to 46° C., was still sufficiently strong to kill mice, but had little effect on guinea-pigs and sheep. A culture twelve days old killed guinea-pigs, but not sheep. It proves fatal to sheep up to six days of cultivation. Their views in reference to the cause of attenuation differ from Pasteur's, who regards oxygen as the active agent, while these observers attribute it exclusively to the high temperature. They succeeded, like Pasteur, by using attenuated cultures in protecting, in most cases, sheep against the action of virulent cultures. In his practical work Pasteur uses two strengths of mitigated virus. The milder vaccine is a culture fifteen to twenty days old; the stronger vaccine is from ten to twelve days old. Sheep are inoculated first with the milder vaccine, and after an interval of twelve to fifteen days the stronger culture is used. Animals thus treated are either entirely immune to anthrax, or, if they contract the disease, it assumes a mild type. Other methods of attenuation of active cultures to be used for prophylactic inoculations have been devised, but, as they appear to have been put only to a limited extent to practical tests, they will be only briefly mentioned here. Sanderson found that the bacillus of anthrax loses much of its virulence when passed through the system of a guinea-pig. Toussaint and Chaveau found that the action of a temperature of from 50° to 55° C., continued for five to twenty minutes, greatly diminishes the virulence of the bacillus of anthrax. For the attenuation of spores a temperature of 80° C. is required.

Paul Bert showed that oxygen, under a pressure of from 20 to 40 centimetres, destroys the bacillus of anthrax. Toussaint, Chamberland and Roux, and Klein made experiments to determine the influence of chemical agents in effecting attenuation of active cultures, and their work has shown that the virulence of some bacteria can be greatly diminished and even entirely suspended by this method of treatment. Arloing asserts that anthrax bacilli, exposed to a bright sunlight in a liquid medium, gradually part with their toxic qualities. More accurate knowledge and greater experience in this interesting field of prophylactic inoculations will undoubtedly lead to important results in the near future.

THERAPEUTIC INOCULATION.

Therapeutic inoculations have been put to a practical test upon a knowledge obtained from laboratory work, that direct antagonism exists among certain kinds of micro-organisms. Emmerich's experiments on rabbits have demonstrated the value of the streptococcus of erysipelas as a protective and curative agent in anthrax in these animals. In one series of experiments the rabbits were first inoculated with a large quantity of a reliable culture of the microbe of erysipelas, and then, two to fourteen days later, the animals were infected with a pure culture of the anthrax bacillus. Of 15 animals treated in this way, 7 recovered, while all the control animals inoculated only with anthrax died; of the 7 animals which died after double infection, some succumbed to the anthrax bacillus and some to the streptococcus of erysipelas. Therapeutic inoculations with cultures of the microbe of erysipelas in animals suffering from anthrax were less successful. Garré has studied antagonism among bacteria on culture soils. He made many careful experiments to determine the growth of a culture on different nutrient media, by removal of the entire culture with a minute spade and inoculation of the same soil with another microbe. From the results obtained thus far he has ascertained that some microbes affect the soil favorably for the growth of other varieties, while others render it sterile. For example, a culture medium impregnated with the ptomaines of the bacillus fluorescens putidus remains perfectly sterile when inoculated with pus-microbes. These investigations have an important practical bearing, as future research may not only show the way to secure immunity from infection by pathogenic microbes by prophylactic inoculations with harmless microbes, but may likewise establish a system of rational and effective treatment by inoculations of cultures of antagonistic bacteria for therapeutic purposes. Therapeutic inoculations with potent cultures have also been made with some success in the treatment of inoperable malignant tumors. In a recent publication on this subject Bruns gives the result of 22 cases of malignant growths, including 1 that came under his own observation that passed through an attack of erysipelas. Bruns's case was one of melanosarcoma of the breast, in which a final cure followed the attack. Out of 5 sarcomata, 3 were permanently cured, while the other 2 were diminished in size, but soon returned to their former size. The effect of the erysipelatous invasion proved negative in 6 cases, in which the diagnosis between carcinoma and sarcoma could not be positively made, as also in 3 cases of ulcerative epithelioma. It is stated that in cicatricial keloid and lymphomata the attack of erysipelas proved curative.

BACTERIA OUTSIDE OF THE BODY.

Bacteriology has rendered the term *miasma* obsolete. All infective diseases are now traced to an organic contagium. Most of the bacteria are ectogenous; that is, they exist, and, under favorable circumstances, multiply outside of the body. The microbe of syphilis, in all probability, is an endogenous parasite. Auto-infection is a misapplied term, as nearly all, if not all, infective diseases are caused by the introduction into the body of pathogenic bacteria from without. Some microbes exist in the soil, and as they or their spores may exist in an active condition for an indefinite period of time, or even germinate there, they give rise to endemics of infective diseases. The anthrax bacillus, the bacillus of tetanus, and the actinomyces can be included in this category. Other microbes are diffused over large territories through water-courses, as the bacillus of typhoid fever and cholera. Finally, some bacteria, like pus-microbes, appear to be ubiquitous, being present everywhere and at all times. Of all substances which serve as a carrier of microbes, the atmospheric air is the most important, because it is present everywhere on the surface of the globe, and no one can exclude himself from it. In a dry state, pathogenic bacteria move with the currents of air and attach themselves again to the solid or fluid substances with which they come in contact. Although most of the pathogenic bacteria under ordinary circumstances do not reproduce themselves outside the body, their resistance to heat and cold, moisture and dryness, is so great that they retain their disease-producing qualities often for an indefinite period of time, and after their entrance into the body, and meeting with a proper nutrient medium, they exert their specific pathogenic effects. *From a practical stand-point it is important to remember that infection takes place by the entrance into the tissues or body of micro-organisms from without, through some defect of the skin or mucous membranes, hence by contact entrance of bacteria into the body.* As a rule, to which there are few exceptions, bacteria are introduced into the body through a wound, abrasion, or ulceration of the skin or a mucous membrane. Such a defect or gateway is called an *infection-atrium*. A healthy, granulating surface furnishes almost as secure a protection against infection as the skin, but when the granulations are destroyed or injured infection is again liable to occur. On this account probing of a fistulous canal has not infrequently resulted in aggravation of the local symptoms, and even in general infection. Küster reports 2 cases where patients who had undergone an operation for hydrocele by incision, and who were permitted to leave the hospital before the wound had completely healed, died subsequently from sepsis caused by careless after-treatment of the granulating surface. Most of the microbes, after they have become deposited upon an absorbing surface, exercise first their pathogenic qualities at the seat of primary localization. The action of some of them always remains local. If the infection spread, it does so by dissemination of the microbes over a surface, along the connective tissue, or through the lymphatics or blood-vessels. There is no reason to doubt that bacteria can gain entrance into the tissues and the circulation by passing through intact mucous membranes in the same manner as minute particles of inorganic material, like coal-, marble-, and ivory-dust. This brings up the question of the

PRESENCE OF PATHOGENIC BACTERIA IN THE HEALTHY BODY.

It still remains a disputed question whether pathogenic micro-organisms can exist in the body without giving rise to disease. It has been definitely ascertained, by experimental research, that many of the pathogenic microbes are harmless as long as they remain in the circulating blood, and that their specific pathogenic action only becomes evident after localization has taken place in some part of the body, in a soil prepared by injury or disease for their reproduction. It has also been conclusively shown, by clinical experience, that pathogenic spores may remain in the healthy body, in a dormant condition, for an indefinite period of time, until, by some accidental pathological changes, the tissues in which they may exist have been prepared for their germination. Numerous experiments will be cited elsewhere, in which injections of pure cultures directly into the circulation produced no ill effects in

healthy animals, but when previous to the injection, or soon after, an injury was inflicted in some part of the body, localization occurred at the seat of trauma, and in the *locus minoris resistentiæ* thus created the microbes produced their specific pathogenic effects. From these remarks it is reasonable to assume *that pathogenic microbes may and do exist in the healthy body without necessarily giving rise to disease, especially if, as is well known, they are being constantly eliminated through the excretory organs.*

Bizzozero could not detect bacteria of any kind in animals soon after birth, but in the lymph-follicles of the cæcum in healthy rabbits he found numerous micro-organisms. They were seen mostly in the protoplasm of cells,—a condition which would indicate that they are transferred from the intestinal canal into the closed lymph-follicle through the medium of migrating cells. In the human subject, Ribbert found micro-organisms in the interior of the epithelia lining the intestinal canal, but they were absent in the submucosa. Perhaps the epithelial cells in this locality take the part of phagocytes. Zahor examined the blood, testicle, heart, and spleen of a healthy rabbit, and found in fresh as well as in hardened sections, after staining with methyl-violet, cocci, and here and there rods. The same examinations, with like results, were made on the organs of a young cat. Fodor introduced directly into the circulation of rabbits pathogenic bacteria, in order to study their effects on the tissues and manner of elimination. As a rule, he found they had completely disappeared from the blood after twenty-four hours. He believes that the bacteria are destroyed in the circulation by the blood-corpuscles. The same author maintains that the power of the blood to destroy bacteria is not diminished by a moderate degree of anæmia, but is lessened when diluted with water, as, when this is done, the microbes are destroyed more slowly and with greater difficulty. Watson-Cheyne found, in his experiments made for the purpose of ascertaining the presence of micro-organisms in the living tissues, that while they were not present when the animal was in good condition, yet if the vitality of the animal was depressed, say, by administering large doses of phosphorus for some time, microbes could be found at times in the blood and tissues of the body. Again, it has been found that, while some micro-organisms when introduced into the living body in small number disappear after a short time, when a large quantity of the culture is introduced the tissues of the body are injured by the pre-existing ptomaines and the microbes retain their vitality and often cause inflammation of the organ in which they locate. The conditions, then, upon which depend the preservation of health in the event of the entrance of pathogenic microbes into the body, are: 1. The number of microbes introduced. 2. Absence of a *locus minoris resistentiæ*. 3. Active elimination through the excretory organs.

LOCALIZATION OF BACTERIA.

Every surgeon has had frequent opportunities to observe cases in which a slight subcutaneous injury was followed by a destructive inflammation,—an inflammation not caused by the trauma alone, but by the trauma giving rise to localization of pathogenic microbes in the tissues altered by the injury. Thus, Chaveau has shown experimentally that a subcutaneous contusion furnishes an excellent condition for the localization of pathogenic bacteria carried to the part by the circulating blood. When he injected a putrid fluid directly into the circulation of young rams shortly before crushing subcutaneously one of the testicles, the injured organ always became the seat of septic gangrene, while without such injection the testicle disappeared completely by necrobiosis and absorption. Gangrene only occurred if the putrid fluid contained bacteria; it did not take place when the injected fluid had been sterilized by filtration. Extensive subcutaneous injuries, as severe contusions, rupture of tendons or muscles, and comminuted fractures, are not followed by suppuration unless the injured tissues become subsequently the seat of infection with pus-microbes. A patient may have been the subject of tubercular infection for an indefinite period of time, and yet may present the appearances of ordinary health, until some slight injury determines localization of the bacillus in the part injured,—an occurrence which is followed by a localized tuberculosis from which, later, regional and general dissemination takes place, to which the patient finally succumbs, unless the tubercular focus is removed by an early operation. *These facts suggest very strongly that, in the hypothetical cases, suppuration and tuberculosis would not have occurred in the part injured without the injury, and that the injury certainly would not have produced suppuration or tuberculosis unless the respective patients had been infected previously with specific micro-organisms.* The injury in these cases created a so-called *locus minoris resistentiæ*, which may signify one of two things: (1) Diminution or suspension of the vital resistance on the part of the injured tissues to the action of pathogenic microbes; or (2) the injury so alters the tissues that bacteria, which were present in the circulation without having given rise to symptoms, become arrested, and find at the same time at the seat of localization the necessary conditions for their reproduction. Heuber studied experimentally the effect of chemical irritation of tissues in determining localization of the bacillus of anthrax. The experiments were made on rabbits. in which by the external application of croton-oil to the ear he produced a tissue-lesion by the inflammation which followed. One ear was thus treated, the other being left in a normal condition in order to compare the results of localization of anthrax bacilli in inflamed and normal

vessels. As soon as the inflammation was established, a pure culture of anthrax bacilli was inserted subcutaneously at the root of the tail; this place was selected in order to make the infection as far as possible from the inflamed ear. In some cases the croton-oil was applied after the inoculation. Immediately after the death of the animal, both ears were cut off and carefully preserved for subsequent examination, and, at the same time, serum and blood were separately taken from the inflamed ear and preserved in sterilized glass tubes.

The results of a number of these experiments enabled the author to assert that in all stages of the inflammation the bacilli were never found outside the walls of the capillary blood-vessels in the crotonized ear. Their number within the blood-vessels depended upon the condition of the inflamed vessels. During the first stage of inflammation, marked by œdema without suppuration, more bacilli were found within the inflamed vessels than in the corresponding vessels of the opposite ear. During the suppurative stage the bacilli disappeared from the vessels. During the third stage, when granulations commenced to form, a complete change was again observed in the bacteriological condition of the inflamed part. The height of this stage is reached on the tenth day. During this stage the bacilli re-appear in the inflamed tissue, where they can be seen in considerable number, especially in the interior of new capillary vessels. During cicatrization the number of bacilli in a corresponding area of both ears was about the same.

From these observations the author concludes that the bacillus of anthrax finds, in a soil prepared by inflammatian induced with croton-oil, a *locus minoris resistentiæ*, which presents more favorable conditions for its localization and growth than the tissues in other parts of the body. Suppuration appeared to neutralize the anthracic process by the destructive effect of the pus-ptomaines upon the bacilli.

The conclusions which he has drawn from his experiments may be summarized as follows: Localization of pre-existing micro-organisms in tissues prepared by injury or disease takes place, provided that the necessary conditions for their growth are present. In looking over different pathological conditions we frequently meet with a so-called *locus minoris resistentiæ*; at any rate, if we search only for that which should mean what has been described above, it is not difficult to conceive how slight injuries, wounds, contusions, etc., should in this manner give rise to serious affections. But not only do direct tissue-lesions, as hæmorrhage, necrosis, hyperæmia, fractures, etc., act in this manner, but a variety of pathological conditions of a general nature may serve the same purpose, as imperfect digestion, enfeebled circulation and respiration, and particularly irregular distribution of blood resulting from xposure to cold. All these ill-defined conditions belong here, and rough their instrumentalities the localization of infective microbes is vored. In secondary or mixed infection the microbes which exist in ie tissues first prepare the soil for the arrest and germination of other icteria which may reach the circulation.

Muskatblüth studied experimentally the fate of anthrax bacilli when troduced directly into the trachea by injection through the larynx, or rough a tracheotomy wound. From the results which he obtained he ncludes that the bacilli can enter the circulation through the bronchial ucous membrane, and that the juice-canals and lymphatics are the iannels through which the infection takes place. It appeared strange the author that no bacilli could be found in leucocytes, but always ıly in epithelial cells. Final localization of the bacilli which have ıtered the circulation through the lungs takes place in distant organs y implantation upon the endothelial lining of the capillary vessels.

Other experimenters affirm that if the anthrax bacilli are injected in oderate quantities into the circulation of animals, they disappear soon om the blood without having produced any pathogenic effects; but, if animals thus infected a contusion is produced in some part of the ody, the bacilli pass out of the injured vessels into the connective tissue ong with the blood, germinate there, and soon cause the formation of ie characteristic inflammatory product, the disease becomes diffused, id the animals die of anthrax. Localization of the bacillus of tubercusis affords an interesting subject for experimental research and clinical udy.

The late distinguished Professor von Volkmann, from an extensive inical experience, came long ago to the important and practical conusion that a severe trauma seldom, if ever, gives rise to tuberculosis the seat of injury; and, on the other hand, that in cases where tuberılosis develops in consequence of any injury, the trauma is always ight, sometimes almost insignificant. The experience of almost every ırgeon will agree with these statements. Volkmann maintains that the tive tissue changes which follow a severe trauma during the reparative ocess counteract the growth and propagation of the bacillus. Luecke tributes to exposure to cold an important rôle in the causation of bercular and other infective forms of inflammation, as he asserts that e sudden diminution of blood-supply to the cutaneous surface causes ternal congestions, which favor the localization of pathogenic microbes some one of the congested organs, otherwise predisposed to the specific flammation. Schüller studied the localization of the tubercular virus perimentally in the same manner as others [illegible] studied the localition of pus-microbes. He inoculated as [illegible] roducts of tubercular inflammation, subsequently produced contusions and sprains of joints, and observed that localization usually occurred at the seat of injury. If the tubercular virus was introduced by inhalation, the same typical lesions occurred in the injured joints as when infection was practiced in a more direct manner. In all cases the product of the local joint-lesion corresponded with the character of the material introduced through some remote point. Surgeons are well aware of the danger of general infection following an injury to a part or an organ the seat of local tuberculosis, more particularly in cases of tubercular disease of joints treated by *brisement forcé*. Numerous cases are recorded where this procedure was followed within a few days by general miliary tuberculosis and a speedy death. In all cases where a local tuberculosis develops in consequence of an injury, we must take it for granted that the injured part contained the essential cause of the disease, the bacillus of Koch, and that the lesions caused by the trauma created the necessary conditions for its reproduction; or, if the injured tissues at the time are sterile, that they serve the purpose of a *locus minoris resistentiæ* for bacilli which might reach them through the circulation. The frequency with which suppuration occurs without any visible *infection-atrium* has led bacteriologists to investigate with special care and diligence localization of pus-microbes.

Rosenbach ascertained, by numerous experiments, that acute suppurative osteomyelitis could only be produced by injecting pus-microbes directly into the circulation and by injuring the medullary tissue a few days before or after the inoculation. Kocher, Becker, and Krause repeated the experiments of Rosenbach, and came essentially to the same conclusions. Both Kocher and Rosenbach look upon the altered circulation in the injured part as the essential condition which determines localization of the pus-microbes floating in the blood-current; at the same time they admit that the immediate tissue-lesions, hæmorrhage, and necrosis may have the same effect. Upon the same theory, Kocher explains the occurrence of traumatic suppurative strumitis in a hyperplastic struma. If non-septic pus is injected into the circulation of healthy animals in moderate quantities no serious results are produced, as the pus-microbes are soon eliminated through the kidneys. If, however, the pus-microbes attach themselves in the circulation to some foreign substance which prevents such elimination, suppuration will follow. A number of experiments made, among others by Ribbert, on the production of myo- and endo- carditis in rabbits, have shown that abscesses can be produced in other organs if the pyogenic microbes are attached to foreign bodies which cannot pass through the pulmonary capillaries. Thus, Ribbert was able to produce myocarditis by using a cultivation of staphylococcus pyogenes aureus on potato, if he took the precaution, in removing the culture from the surface of the potato, to scrape off also the superficial surface of the potato itself. The particles of potato injected with the microbes determined suppuration by causing localization of the microbes, as the foreign bodies were too large to pass through the capillary vessels and were not capable of removal by absorption.

The influence of a trauma in determining localization of microbes circulating in the blood is well shown by the experiments which have been made to produce, artificially, endocarditis in animals. O. Rosenbach made the first experiments of this kind. He observed, in his experiments on animals and in post-mortem examinations in cases of ulcerative endocarditis, microbic emboli in the valves of the heart and in the infarcts of other organs, and classifies this affection with pyæmia. The more frequent occurrence of endocarditis in the left side of the heart than the right he explains by assuming that the microbes find a better soil in the arterial blood, as when the affection occurs in the fœtus during intra-uterine life, when the blood in both sides of the heart is of about the same composition, the valves in both sides are affected with the same frequency. Orth and Wyssokowitsch found that staphylococci could be injected into the blood of a rabbit without apparent injury to it, but if before the injection a slight mechanical injury was inflicted on one of the valves of the heart, typical endocarditis was at once produced. The injury was produced with a small rod, which was introduced into the jugular vein on the right side. The endocardial lesion always corresponded to the seat of the injury. Similar results were obtained by Fränkel and Sänger.

Rinne came to different conclusions in reference to injured tissues serving as a *locus minoris resistentiæ* in the causation of inflammation due to the presence of microbes. He injected pure cultures of the different kinds of pus-microbes directly into the circulation of animals, and found that, as a rule, no harm resulted. In rabbits he injected from 2 to 3 Pravaz syringefuls of unfiltered, distilled water, holding in suspension pure cultures, and, after repeating this dose several times, inflicted all kinds of subcutaneous lesions without causing suppuration. Only in a few instances were pyæmic metastases observed, and these occurred usually only in cases where undiluted gelatin cultures were used. In several dogs he made subcutaneous fractures and then injected large doses of cultures of pus-microbes, suspended in distilled water, into the peritoneal cavity, but no suppuration occurred at the seat of trauma. In six rabbits he fractured the femur subcutaneously and then injected pure cultures into the jugular, or one of t [illegible] veins, but only in one of them did osteomyelitis occur at the seat of fracture. In two experiments where he injected osteomyelitic pus diluted with distilled water the seat of fracture suppurated, and in these cases abscesses were also found in the heart-muscle and the kidneys at the autopsy. It is difficult to explain the discrepancy between the results obtained by Rinne and the other experimenters who have been quoted, as the same kind of animals and inoculation material were used, and the experiments were conducted in the same manner. *The fact remains, and is abundantly vouched for by clinical experience, that a subcutaneous injury, if the tissues remain sterile, does not give rise to inflammation, and that many inflammatory processes are established immediately or soon after an injury, and in the inflammatory product the presence of pathogenic microbes can be demonstrated by microscopical examination, cultivation, and inoculation experiments.* A number of well-authenticated cases of osteomyelitis after simple subcutaneous fracture have been recorded where the infection could be traced to a slight peripheral suppurative lesion. The same can be said of many cases of suppurative osteomyelitis which occur without fracture, where the exciting cause can be referred to some slight injury, or exposure to cold, and the essential cause can be located in some pus-producing lesion in a distant part, and having no direct vascular connections with the suppurating medullary tissue. *From a scientific and practical stand-point, it is important to recognize the existence of local conditions in the tissues created by a trauma, or antecedent pathological conditions, to explain the localization of floating microbes and the production of local affections by their uniform presence and constant pathogenic action.*

SECONDARY OR MIXED INFECTION.

Antecedent pathological products may serve the same purpose in the body as a trauma in the determination of localization of pathogenic microbes. Suppuration in a tumor, or a hyperplastic gland with an intact cutaneous covering, indicates that in the tumor or swelling pus-microbes have been arrested, and that they have been deposited in a soil adapted to their germination and the exercise of their pathogenic qualities. The atypical vascularization in tumors and the partial obstruction in the lumen of blood-vessels in inflammatory swellings cannot fail in creating conditions which determine filtration of bacteria-containing blood. If the pre-existing pathological product is the result of a previous infection, and serves as a medium for localization of another kind of pathogenic microbes, we speak of the combined process due to the presence of two varieties of micro-organisms as a mixed infection. The first positive proof of the existence of a secondary or mixed infection was furnished by Brieger and Ehrlich. These observers saw a malignant œdema develop at the point where musk was injected hypodermatically in a severe case of typhoid fever. They found that in such cases a predisposition is established by an existing disease to the growth and reproduction of micro-organisms, which may have been previously present in the organism without producing any pathological lesions.

Koch, in his article on "The Etiology of Tuberculosis," alludes to the occurrence of mixed infection, as he states that he saw at the same time bacilli and micrococci present in the same tubercular lesion. In reference to the occurrence of micrococci in tubercular deposits in the lungs and spleen, he explained their presence upon the supposition that they entered the circulation through ulcerations of the tongue. and that they became arrested in the capillary vessels, which had lost their normal resisting power by the tubercular process. Bumm maintains that in some patients secondary infection is a purely accidental occurrence, as, for example, a tuberculous patient can be attacked with erysipelas; a lying-in woman suffering from gonorrhœa may become the subject of septic infection.

Another and practically more important variety of mixed infection he speaks of where a more direct relation exists between the different microbes, in the sense that the one precedes the other and prepares the soil for the growth of the latter. These forms are characterized by being constantly associated with certain definite microbes. The pneumococcus may prepare the soil for fructification of the bacillus of tuberculosis or the microbes of suppuration in individuals that otherwise would have been immune to the action of these micro-organisms. The gonococcus can also modify the mucous membrane of the genito-urinary tract in such a manner as to render easy the invasion of other pathogenic microbes. Gonorrhœal infection of the vulvo-vaginal gland furnishes a good illustration. As long as the infection remains purely gonorrhœal, the acute suppurative stage is followed by a chronic stage which may last for several months, the swelling gradually subsides, and subsequently atrophy and sclerosis of the gland follow. If, however, purulent infection is added to the gonorrhœa, the gland soon becomes enlarged and tender, and suppuration follows. In the abscess and its vicinity no gonococci can be found; the pus only contains pyogenic microbes, which exterminated the gonococci. Cystitis which accompanies gonorrhœa is, again, a variety of mixed infection. The stratified epithelium of the bladder is impenetrable to the gonococcus.

According to Bumm the cystitis is maintained by another species of microbe resembling the gonococcus, but differing from it by taking a

healthy animals, but when previous to the injection, or soon after, an injury was inflicted in some part of the body, localization occurred at the seat of trauma, and in the *locus minoris resistentiæ* thus created the microbes produced their specific pathogenic effects. From these remarks it is reasonable to assume *that pathogenic microbes may and do exist in the healthy body without necessarily giving rise to disease, especially if, as is well known, they are being constantly eliminated through the excretory organs.*

Bizzozero could not detect bacteria of any kind in animals soon after birth, but in the lymph-follicles of the cæcum in healthy rabbits he found numerous micro-organisms. They were seen mostly in the protoplasm of cells,—a condition which would indicate that they are transferred from the intestinal canal into the closed lymph-follicle through the medium of migrating cells. In the human subject, Ribbert found micro-organisms in the interior of the epithelia lining the intestinal canal, but they were absent in the submucosa. Perhaps the epithelial cells in this locality take the part of phagocytes. Zahor examined the blood, testicle, heart, and spleen of a healthy rabbit, and found in fresh as well as in hardened sections, after staining with methyl-violet, cocci, and here and there rods. The same examinations, with like results, were made on the organs of a young cat. Fodor introduced directly into the circulation of rabbits pathogenic bacteria, in order to study their effects on the tissues and manner of elimination. As a rule, he found they had completely disappeared from the blood after twenty-four hours. He believes that the bacteria are destroyed in the circulation by the blood-corpuscles. The same author maintains that the power of the blood to destroy bacteria is not diminished by a moderate degree of anæmia, but is lessened when diluted with water, as, when this is done, the microbes are destroyed more slowly and with greater difficulty. Watson-Cheyne found, in his experiments made for the purpose of ascertaining the presence of micro-organisms in the living tissues, that while they were not present when the animal was in good condition, yet if the vitality of the animal was depressed, say, by administering large doses of phosphorus for some time, microbes could be found at times in the blood and tissues of the body. Again, it has been found that, while some micro-organisms when introduced into the living body in small number disappear after a short time, when a large quantity of the culture is introduced the tissues of the body are injured by the pre-existing ptomaines and the microbes retain their vitality and often cause inflammation of the organ in which they locate. The conditions, then, upon which depend the preservation of health in the event of the entrance of pathogenic microbes into the body, are: 1. The number of microbes introduced. 2. Absence of a *locus minoris resistentiæ.* 3. Active elimination through the excretory organs.

LOCALIZATION OF BACTERIA.

Every surgeon has had frequent opportunities to observe cases in which a slight subcutaneous injury was followed by a destructive inflammation,—an inflammation not caused by the trauma alone, but by the trauma giving rise to localization of pathogenic microbes in the tissues altered by the injury. Thus, Chaveau has shown experimentally that a subcutaneous contusion furnishes an excellent condition for the localization of pathogenic bacteria carried to the part by the circulating blood. When he injected a putrid fluid directly into the circulation of young rams shortly before crushing subcutaneously one of the testicles, the injured organ always became the seat of septic gangrene, while without such injection the testicle disappeared completely by necrobiosis and absorption. Gangrene only occurred if the putrid fluid contained bacteria; it did not take place when the injected fluid had been sterilized by filtration. Extensive subcutaneous injuries, as severe contusions, rupture of tendons or muscles, and comminuted fractures, are not followed by suppuration unless the injured tissues become subsequently the seat of infection with pus-microbes. A patient may have been the subject of tubercular infection for an indefinite period of time, and yet may present the appearances of ordinary health, until some slight injury determines localization of the bacillus in the part injured,—an occurrence which is followed by a localized tuberculosis from which, later, regional and general dissemination takes place, to which the patient finally succumbs, unless the tubercular focus is removed by an early operation. *These facts suggest very strongly that, in the hypothetical cases, suppuration and tuberculosis would not have occurred in the part injured without the injury, and that the injury certainly would not have produced suppuration or tuberculosis unless the respective patients had been infected previously with specific micro-organisms.* The injury in these cases created a so-called *locus minoris resistentiæ*, which may signify one of two things: (1) Diminution or suspension of the vital resistance on the part of the injured tissues to the action of pathogenic microbes; or (2) the injury so alters the tissues that bacteria, which were present in the circulation without having given rise to symptoms, become arrested, and find at the same time at the seat of localization the necessary conditions for their reproduction. Heuber studied experimentally the effect of chemical irritation of tissues in determining localization of the bacillus of anthrax. The experiments were made on rabbits, in which by the external application of croton-oil to the ear he produced a tissue-lesion by the inflammation which followed. One ear was thus treated, the other being left in a normal condition in order to compare the results of localization of anthrax bacilli in inflamed and normal

vessels. As soon as the inflammation was established, a pure culture of anthrax bacilli was inserted subcutaneously at the root of the tail; this place was selected in order to make the infection as far as possible from the inflamed ear. In some cases the croton-oil was applied after the inoculation. Immediately after the death of the animal, both ears were cut off and carefully preserved for subsequent examination, and, at the same time, serum and blood were separately taken from the inflamed ear and preserved in sterilized glass tubes.

The results of a number of these experiments enabled the author to assert that in all stages of the inflammation the bacilli were never found outside the walls of the capillary blood-vessels in the crotonized ear. Their number within the blood-vessels depended upon the condition of the inflamed vessels. During the first stage of inflammation, marked by œdema without suppuration, more bacilli were found within the inflamed vessels than in the corresponding vessels of the opposite ear. During the suppurative stage the bacilli disappeared from the vessels. During the third stage, when granulations commenced to form, a complete change was again observed in the bacteriological condition of the inflamed part. The height of this stage is reached on the tenth day. During this stage the bacilli re-appear in the inflamed tissue, where they can be seen in considerable number, especially in the interior of new capillary vessels. During cicatrization the number of bacilli in a corresponding area of both ears was about the same.

From these observations the author concludes that the bacillus of anthrax finds, in a soil prepared by inflammatian induced with croton-oil, a *locus minoris resistentiæ*, which presents more favorable conditions for its localization and growth than the tissues in other parts of the body. Suppuration appeared to neutralize the anthracic process by the destructive effect of the pus-ptomaines upon the bacilli.

The conclusions which he has drawn from his experiments may be summarized as follows: Localization of pre-existing micro-organisms in tissues prepared by injury or disease takes place, provided that the necessary conditions for their growth are present. In looking over different pathological conditions we frequently meet with a so-called *locus minoris resistentiæ;* at any rate, if we search only for that which should mean what has been described above, it is not difficult to conceive how slight injuries, wounds, contusions, etc., should in this manner give rise to serious affections. But not only do direct tissue-lesions, as hæmorrhage, necrosis, hyperæmia, fractures, etc., act in this manner, but a variety of pathological conditions of a general nature may serve the same purpose, as imperfect digestion, enfeebled circulation and respiration, and particularly irregular distribution of blood resulting from exposure to cold. All these ill-defined conditions belong here, and through their instrumentalities the localization of infective microbes is favored. In secondary or mixed infection the microbes which exist in the tissues first prepare the soil for the arrest and germination of other bacteria which may reach the circulation.

Muskatblüth studied experimentally the fate of anthrax bacilli when introduced directly into the trachea by injection through the larynx, or through a tracheotomy wound. From the results which he obtained he concludes that the bacilli can enter the circulation through the bronchial mucous membrane, and that the juice-canals and lymphatics are the channels through which the infection takes place. It appeared strange to the author that no bacilli could be found in leucocytes, but always only in epithelial cells. Final localization of the bacilli which have entered the circulation through the lungs takes place in distant organs by implantation upon the endothelial lining of the capillary vessels.

Other experimenters affirm that if the anthrax bacilli are injected in moderate quantities into the circulation of animals, they disappear soon from the blood without having produced any pathogenic effects; but, if in animals thus infected a contusion is produced in some part of the body, the bacilli pass out of the injured vessels into the connective tissue along with the blood, germinate there, and soon cause the formation of the characteristic inflammatory product, the disease becomes diffused, and the animals die of anthrax. Localization of the bacillus of tuberculosis affords an interesting subject for experimental research and clinical study.

The late distinguished Professor von Volkmann, from an extensive clinical experience, came long ago to the important and practical conclusion that a severe trauma seldom, if ever, gives rise to tuberculosis at the seat of injury; and, on the other hand, that in cases where tuberculosis develops in consequence of any injury, the trauma is always slight, sometimes almost insignificant. The experience of almost every surgeon will agree with these statements. Volkmann maintains that the active tissue changes which follow a severe trauma during the reparative process counteract the growth and propagation of the bacillus. Luecke attributes to exposure to cold an important rôle in the causation of tubercular and other infective forms of inflammation, as he asserts that the sudden diminution of blood-supply to the cutaneous surface causes internal congestions, which favor the localization of pathogenic microbes in some one of the congested organs, otherwise predisposed to the specific inflammation. Schüller studied the localization of the tubercular virus experimentally in the same manner as others have studied the localization of pus-microbes. He inoculated animals with the products of

healthy animals, but when previous to the injection, or soon after, an injury was inflicted in some part of the body, localization occurred at the seat of trauma, and in the *locus minoris resistentiæ* thus created the microbes produced their specific pathogenic effects. From these remarks it is reasonable to assume *that pathogenic microbes may and do exist in the healthy body without necessarily giving rise to disease, especially if, as is well known, they are being constantly eliminated through the excretory organs.*

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Rosenbach ascertained, by numerous experiments, that acute suppurative osteomyelitis could only be produced by injecting pus-microbes directly into the circulation and by injuring the medullary tissue a few days before or after the inoculation. Kocher, Becker, and Krause repeated the experiments of Rosenbach, and came essentially to the same conclusions. Both Kocher and Rosenbach look upon the altered circulation in the injured part as the essential condition which determines localization of the pus-microbes floating in the blood-current; at the same time they admit that the immediate tissue-lesions, hæmorrhage, and necrosis may have the same effect. Upon the same theory, Kocher explains the occurrence of traumatic suppurative strumitis in a hyperplastic struma. If non-septic pus is injected into the circulation of healthy animals in moderate quantities no serious results are produced, as the pus-microbes are soon eliminated through the kidneys. If, however, the pus-microbes attach themselves in the circulation to some foreign substance which prevents such elimination, suppuration will follow. A number of experiments made, among others by Ribbert, on the production of myo- and endo- carditis in rabbits, have shown that abscesses can be produced in other organs if the pyogenic microbes are attached to foreign bodies which cannot pass through the pulmonary capillaries. Thus, Ribbert was able to produce myocarditis by using a cultivation of staphylococcus pyogenes aureus on potato, if he took the precaution, in removing the culture from the surface of the potato, to scrape off also the superficial surface of the potato itself. The particles of potato injected with the microbes determined suppuration by causing localization of the microbes, as the foreign bodies were too large to pass through the capillary vessels and were not capable of removal by absorption.

The influence of a trauma in determining localization of microbes circulating in the blood is well shown by the experiments which have been made to produce, artificially, endocarditis in animals. O. Rosenbach made the first experiments of this kind. He observed, in his experiments on animals and in post-mortem examinations in cases of ulcerative endocarditis, microbic emboli in the valves of the heart and in the infarcts of other organs, and classifies this affection with pyæmia. The more frequent occurrence of endocarditis in the left side of the heart than the right he explains by assuming that the microbes find a better soil in the arterial blood, as when the affection occurs in the fœtus during intra-uterine life, when the blood in both sides of the heart is of about the same composition, the valves in both sides are affected with the same frequency. Orth and Wyssokowitsch found that staphylococci could be injected into the blood of a rabbit without apparent injury to it, but if before the injection a slight mechanical injury was inflicted on one of the valves of the heart, typical endocarditis was at once produced. The injury was produced with a small rod, which was introduced into the jugular vein on the right side. The endocardial lesion always corresponded to the seat of the injury. Similar results were obtained by Fränkel and Sänger.

Rinne came to different conclusions in reference to injured tissues serving as a *locus minoris resistentiæ* in the causation of inflammation due to the presence of microbes. He injected pure cultures of the different kinds of pus-microbes directly into the circulation of animals, and found that, as a rule, no harm resulted. In rabbits he injected from 2 to 3 Pravaz syringefuls of unfiltered, distilled water, holding in suspension pure cultures, and, after repeating this dose several times, inflicted all kinds of subcutaneous lesions without causing suppuration. Only in a few instances were pyæmic metastases observed, and these occurred usually only in cases where undiluted gelatin cultures were used. In several dogs he made subcutaneous fractures and then injected large doses of cultures of pus-microbes, suspended in distilled water, into the peritoneal cavity, but no suppuration occurred at the seat of trauma. In six rabbits he fractured the femur subcutaneously and then injected pure cultures into the jugular, or one of the auricular, veins, but only in one of them did osteomyelitis occur at the seat of fracture. In two experiments where he injected osteomyelitic pus diluted with distilled water the seat of fracture suppurated, and in these cases abscesses were also found in the heart-muscle and the kidneys at the autopsy. It is difficult to explain the discrepancy between the results obtained by Rinne and the other experimenters who have been quoted, as the same kind of animals and inoculation material were used, and the experiments were conducted in the same manner. *The fact remains, and is abundantly vouched for by clinical experience, that a subcutaneous injury, if the tissues remain sterile, does not give rise to inflammation, and that many inflammatory processes are established immediately or soon after an injury, and in the inflammatory product the presence of pathogenic bacteria can be demonstrated by microscopical examination, cultivation, and inoculation experiments.* A number of well-authenticated cases of osteomyelitis after simple subcutaneous fracture have been recorded where the infection could be traced to a slight peripheral suppurative lesion. The same can be said of many cases of suppurative osteomyelitis which occur without fracture, where the exciting cause can be referred to some slight injury, or exposure to cold, and the essential cause can be located in some pus-producing lesion in a distant part, and having no direct vascular connections with the suppurating medullary tissue. *From a scientific and practical stand-point, it is important to recognize the existence of local conditions in the tissues created by a trauma, or antecedent pathological conditions, to explain the localization of floating microbes and the production of local affections by their uniform presence and constant pathogenic action.*

SECONDARY OR MIXED INFECTION.

Antecedent pathological products may serve the same purpose in the body as a trauma in the determination of localization of pathogenic microbes. Suppuration in a tumor, or a hyperplastic gland with an intact cutaneous covering, indicates that in the tumor or swelling pus-microbes have been arrested, and that they have been deposited in a soil adapted to their germination and the exercise of their pathogenic qualities. The atypical vascularization in tumors and the partial obstruction in the lumen of blood-vessels in inflammatory swellings cannot fail in creating conditions which determine filtration of bacteria-containing blood. If the pre-existing pathological product is the result of a previous infection, and serves as a medium for localization of another kind of pathogenic microbes, we speak of the combined process due to the presence of two varieties of micro-organisms as a mixed infection. The first positive proof of the existence of a secondary or mixed infection was furnished by Brieger and Ehrlich. These observers saw a malignant œdema develop at the point where musk was injected hypodermatically in a severe case of typhoid fever. They found that in such cases a predisposition is established by an existing disease to the growth and reproduction of micro-organisms, which may have been previously present in the organism without producing any pathological lesions.

Koch, in his article on "The Etiology of Tuberculosis," alludes to the occurrence of mixed infection, as he states that he saw at the same time bacilli and micrococci present in the same tubercular lesion. In reference to the occurrence of micrococci in tubercular deposits in the lungs and spleen, he explained their presence upon the supposition that they entered the circulation through ulcerations of the tongue, and that they became arrested in the capillary vessels, which had lost their normal resisting power by the tubercular process. Bumm maintains that in some patients secondary infection is a purely accidental occurrence, as, for example, a tuberculous patient can be attacked with erysipelas; a lying-in woman suffering from gonorrhœa may become the subject of septic infection.

Another and practically more important variety of mixed infection he speaks of where a more direct relation exists between the different microbes, in the sense that the one precedes the other and prepares the soil for the growth of the latter. These forms are characterized by being constantly associated with certain definite microbes. The pneumococcus may prepare the soil for fructification of the bacillus of tuberculosis or the microbes of suppuration in individuals that otherwise would have been immune to the action of these micro-organisms. The gonococcus can also modify the mucous membrane of the genito-urinary tract in such a manner as to render easy the invasion of other pathogenic microbes. Gonorrhœal infection of the vulvo-vaginal gland furnishes a good illustration. As long as the infection remains purely gonorrhœal, the acute suppurative stage is followed by a chronic stage which may last for several months, the swelling gradually subsides, and subsequently atrophy and sclerosis of the gland follow. If, however, purulent infection is added to the gonorrhœa, the gland soon becomes enlarged and tender, and suppuration follows. In the abscess and its vicinity no gonococci can be found; the pus only contains pyogenic microbes, which exterminated the gonococci. Cystitis which accompanies gonorrhœa is, again, a variety of mixed infection. The stratified epithelium of the bladder is impenetrable to the gonococcus.

According to Bumm the cystitis is maintained by another species of microbe resembling the gonococcus, but differing from it by taking a different staining. The gonococcus expends its action on the superficial layers of the mucous membrane exclusively. Suppurative parametritis following gonorrhœa is analogous to a gonorrhœic bubo, which is always caused by a secondary infection with pus-microbes. A valuable contribution to our knowledge of mixed infection has recently been made by Babes. His investigations consist of a series of bacteriological studies of the tissues of children who died of infectious diseases. Within a few hours after death fragments of tissue were removed from different organs which, under strict antiseptic precautions, were imbedded in sterilized culture material. In acute infectious diseases, such as diphtheria and scarlatina, cultures from the spleen, kidneys, liver, lungs, and blood yielded numerous colonies of streptococci, putrefactive bacteria, capsule cocci, more rarely staphylococci and various bacilli. Of special interest are his researches on the manner of localization and extension of the secondary invasion after different primary diseases. In 8 cadavers he found one or more species of bacteria in the internal organs. In a case of septic omphalitis he found the bacillus of green pus. In 6 cases of different forms of infectious disease the streptococcus pyogenes could be cultivated from the tissues, and only in 1 was the yellow pus-microbe present in the culture. Various putrefactive bacilli were cultivated from 5 cases. In some instances he was able to demonstrate the point at which the different secondary invasions had taken place. Thus, in a case of sepsis after scarlatina, in which streptococci were found in every part of the body, a streptococcus pneumoniæ was found in the lower portion of the left lung, while a number of foci in the upper portion of the opposite lung contained only bacilli.

Fränkel and Freudenberg cultivated from internal organs of 3 patients who had died of scarlatina the streptococcus pyogenes, and they maintain that the presence of this microbe is evidence that a secondary infection takes place through the diseased mucous membrane of the pharynx.

Schnitzler, after having observed and carefully studied a number of cases, has come to the conclusion that syphilitic ulcerations of the larynx may pass into tubercular, as the syphilitic ulcer furnishes a good culture soil for the bacillus of tuberculosis.

Heuber attributes the occurrence of suppuration and gangrene in croupous pneumonia, phlegmonous inflammation and suppuration in erysipelas, and suppuration in tubercular processes to secondary infection with pus-microbes. As the bacillus of tuberculosis and the streptococcus of erysipelas do not possess the property of converting leucocytes and embryonal cells into pus-corpuscles, suppuration, if it does occur in these diseases, can only be accounted for by admitting the existence of a secondary infection with pus-microbes.

The important question presents itself whether, in cases of mixed infection, the two or more kinds of microbes enter the organism at the same time, or whether primary infection prepares the way for the entrance and fructification of the microbes which produce the secondary infection. Pus-microbes being present at all times and everywhere, and perhaps gaining entrance into the body more readily than others, it is very easy to understand why secondary infection by them is most frequently observed. Rosenbach frequently found in pus more than one kind of pyogenic microbe. He often cultivated from the same pus two kinds of staphylococci, or one variety of staphylococci with streptococci. While antagonism among some bacteria has been shown to exist, others prepare the soil for the growth of a different variety, and in such instances it is not difficult to conceive that secondary infection is of frequent occurrence. For instance, any microbe that will convert mature tissue into embryonal cells abbreviates and lightens the work of pus-microbes in converting fixed tissue-cells into pus-corpuscles.

ELIMINATION OF PATHOGENIC BACTERIA.

Having described the different ways in which pathogenic bacteria enter the body, it now remains to show in what manner they are disposed of in the event no harm follows, or the patient recovers from the disease which they produced. The probable existence of disease-producing micro-organisms in the healthy body and the spontaneous subsidence of many infective processes make it important to consider the ways and means by which they are rendered harmless in the living body, or are removed by elimination through some of the excretory organs. In all infective processes in which life is not destroyed, and the products of inflammation do not find their way to the surface spontaneously or by operative treatment, the microbes are either destroyed in the blood and the tissues by phagocytosis or are eliminated through some of the excretory organs in an active state. The rapid disappearance of most microbes from the blood when injected into the circulation of healthy animals would indicate that an active warfare is instituted against them by the colored corpuscles of the blood, in which the microbes are defeated,—that is, destroyed. If some of the microbes pass through the capillary blood-vessels and come in direct contact with the fixed tissue-cells, a similar struggle ensues between them and the tissue-cells, and if the latter are victorious the microbes are destroyed. Successful phagocytosis must therefore be considered as the most efficient and desirable way of disposing of pathogenic bacteria after they have entered the tissues or the general circulation. But should phagocytosis prove unsuccessful in destroying the microbes which have reached the blood, there is still another way in which the unassisted resources of the organism can deal with them successfully, viz., elimination through one or more of the excretory organs. The critical discharges of the ancient authors—profuse sweating, diarrhœa, and copious secretion of urine—in the light of modern science have received a different significance, as they are now regarded as efforts of the *vis medicatrix naturæ* to throw off the cause which produced the disease,—the pathogenic microbes and their ptomaines. The kidneys and the mucous membrane of the intestinal canal are the organs most concerned in the process of elimination. That microbes in an active state are eliminated by the kidneys is shown by various observations, and this is an important point to remember as probably explaining certain cases of pyelitis occurring in patients who have never had any instrument passed, and in whom the urethra and bladder are perfectly normal. The salivary glands, more especially the parotid, occasionally take part in the elimination of pus-microbes, thus offering an explanation of the not infrequent occurrence of abscesses in this gland after suppuration elsewhere. The frequency with which the kidneys are affected in cases of tuberculosis furnishes an evidence that elimination of bacilli takes place through these organs. Philipowicz produced tuberculosis in animals by injecting urine taken from tubercular subjects into the peritoneal cavity. Neumann found the specific microbes in the urine in cases of typhus, septicæmia, and pyæmia. In a case of acute endocarditis and osteomyelitis he cultivated from the urine the staphylococcus pyogenes aureus. He asserts that the micro-organisms which circulate in the blood localize in the capillary vessels of the kidney, where they often cause minute multiple lesions without implication of the entire parenchyma of the organ. Through the altered tissues some of the microbes enter the tubuli uriniferi, and are washed away with the urine. Philipowicz found bacilli in the urine in anthrax and glanders. Schweiger has shown conclusively, by his bacteriological researches, that the urine from scarlatinal patients is contagious; for varicella, typhus recurrens, and malaria the same holds true. Schweiger regards all kidney-lesions occurring in the course of infective diseases of microbic origin. To prove that microbes pass through the kidneys, he cultivated a bacillus which Reimann discovered in the pus of ozæna. This bacillus is stained an intense green color in a culture of gelatin and agar after twenty-four hours. A culture of this bacillus was diluted with a physiological solution of salt and injected directly into the circulation. The experiments were made on a dog, cat, and rabbit. A certain length of time intervened between the injection and the appearance of bacilli in the urine, as though, somewhere on their way, an obstacle had been met with. At first only isolated bacilli were found in the urine, but later on they appeared in larger numbers. Bacteriological examinations of milk have shown that different kinds of pathogenic bacteria are eliminated through the mammary gland. The chapter on Bacteria would not be complete without at least alluding briefly to what is known in reference to

DIRECT TRANSMISSION OF PATHOGENIC BACTERIA FROM PARENTS TO FŒTUS.

That many of the infectious surgical diseases are hereditary has been admitted by the best authorities for a long time, and many theories have been advanced to explain their transmission from parents to child. The modern views on this subject may be narrowed down to two suppositions: 1. Transmission from parents to child of a predisposition to certain diseases. 2. Direct transmission from parents to fœtus of the essential cause of the disease. The supposed hereditary predisposition is interpreted as meaning some congenital anatomical or physiological defects in the tissues, which render the organisms unduly susceptible to the action of post-natal microbic infection. The existence of minute anatomical defects of blood-vessels, lymphatic vessels and glands, connective-tissue spaces, etc., has been advanced in explanation of a greater liability of infection with floating microbes, which enter the circulation after birth.

An inherited defective vital resistance on the part of the tissues to the action of bacteria is also considered by many in the light of a congenital influence in the causation of disease. The above-mentioned conditions are recognized, but no satisfactory, demonstrative, or experimental proofs of their existence have as yet been furnished, and yet the immunity of some animals to certain diseases cannot be explained in any other way than in attributing to the tissues anatomical or physiological properties which protect the organism against the action of certain micro-organisms, which, in other animals not so protected by inherited qualities, produce a serious or fatal disease. Clinical observation also teaches us that a great difference exists among different persons in reference to the degree of susceptibility to the same form of infection. In many persons, for instance, inoculation with a pure culture of tubercle bacilli would be a perfectly harmless procedure; in some it would be followed by a localized tubercular process, which in the course of time might heal spontaneously; while in a few, rendered more susceptible to this form of infection by hereditary or acquired causes, inoculation with the same number of bacilli would be followed by a severe form of local tuberculosis, soon to be followed by regional and general dissemination and death. The same can be said of nearly all, if not all, infectious diseases. *If their existence has not been demonstrated, we are, neverthe-*

less, forced to accept the influence of certain as yet unknown conditions inherent in the tissues, and which are often traceable to a congenital cause or causes, which favor or resist post-natal microbic diseases. During the last few years some progress has been made in showing that hereditary diseases, in many instances at least, are due to a more direct cause—transmission from parents to fœtus of the essential cause of the disease—pathogenic microbes. Although our knowledge of the intra-uterine origin of microbic diseases is as yet imperfect, there can be no doubt that future study and research will clear up many dark points, and furnish satisfactory demonstrative explanations of the direct and indirect hereditary influences in the causation of disease. It is well known that small-pox, measles, and scarlatina are directly transmissible from mother to fœtus. Numerous well-authenticated cases of these diseases occurring in newborn children have been recorded. Lebedeff reports a case of premature birth which occurred eight days after the mother had recovered from erysipelas. The child died ten minutes after birth, and the author found Fehleissen's streptococcus in the lymphatic vessels, in the diseased skin, and in the umbilical cord, but none in the placenta. The author believes that the streptococci were transported from the lymphatic vessels of the lower extremities of the mother through the lymphatics of the uterus into the placental vessels, and from the maternal into the fœtal circulation. Ahlfeld and Marchand report the case of a woman who presented no symptoms of disease except a moderate pallor and tympanitic distention of the abdomen. After a normal labor she gave birth to her second child; eight hours after delivery the patient died in collapse, for which no cause could be found. The autopsy revealed anthrax as the cause of death. The child died four days after birth from the same cause. The mother, as was later ascertained, contracted the disease in sorting horse-hair, and the child was infected directly through the placental circulation. Sangalli found the bacilli of anthrax in the blood of a fœtus from a woman who had died of anthrax. In opposition to Golzi and others, he affirms that the transmission of the disease from mother to fœtus could only have taken place by the passage of the bacilli or spores from the maternal to the fœtal circulation through the placental vessels. Netter reports a carefully-observed case of direct transmission of the diplococcus of pneumonia from mother to fœtus. The mother was a VI-para, pregnant eight months, when she was attacked with croupous pneumonia, which terminated on the seventh day in recovery. On the ninth day after the attack she was delivered of a living child. The child died on the fifth day after birth. The autopsy revealed lobar pneumonia involving the right upper lobe, double fibrinous pleuritis, pericarditis, suppurative meningitis, and otitis media on both sides. Bacteriological examination of the different inflammatory products, as well as of the blood taken from the left ventricle, showed the presence of Fränkel's diplococcus pneumoniæ. One of the strongest evidences of direct transmission of pathogenic microbes from mother to fœtus through the placental circulation is the often-quoted observation made by Johne. An eight months' fœtus was taken from a cow, the subject of advanced tuberculosis. No tuberculous products were found in the placenta or the uterus, but in the lower lobe of the right lung of the fœtus a nodule the size of a pea was detected, containing four caseous centres. The bronchial glands were tubercular. The liver contained numerous miliary nodules, All the lesions presented under the microscope the characteristic histological structure of tubercle. Jani has examined the healthy sexual organs of nine phthisical patients for tubercle bacilli. No bacilli were found, in any of these, in the semen from the vesiculæ seminalis, but, on the other hand, in 5 out of 8 cases, a few were found in the testicle, and in 4 out of 6 in the prostate gland. He further examined two women who died of pulmonary phthisis, the ovaries in both presenting negative results. In one case of chronic pulmonary phthisis, with extensive intestinal tuberculosis, he examined the Fallopian tubes, and found tubercle bacilli. He believes that the tuberculous virus can be transmitted from parents to offspring in one of two ways: 1. Through the semen of the male. 2. Through the migration of bacilli into the uterus from the abdominal cavity. The frequency with which the Fallopian tubes are the seat of tuberculous lesions make it more than probable that the ovum, on its way from the ovaries to the uterine cavity, is infected with bacilli. It also requires no stretch of the imagination to understand how the spermatozoa in the testicle or on its way to the vesiculæ seminalis can be contaminated with bacilli, and thus the disease directly transmitted from father to fœtus.

That syphilis is a microbic disease can no longer be doubted, and that it is one of the diseases which is most frequently transmitted from parents to offspring is well known.

That pathogenic micro-organisms may exist in the blood of apparently healthy mothers without doing any harm is well illustrated by children who have been born suffering from suppurative osteomyelitis, while the mothers, through whose blood only the micro-organisms could have come, showed no evidences of disease. Rosenbach reports such a case in his artice on acute osteomyelitis. Transmission of microbic diseases through the placental circulation has been made the subject of experimental inquiry. Strauss and Chamberland experimented on guinea-pigs to prove that intra-uterine transmission of anthrax from mother to offspring is possible. Gravid animals were inoculated with the virus of anthrax, and the fœtuses examined immediately after death. Blood taken from the cavities of the heart and liver, examined under the microscope, never showed bacilli. Cultivation experiments were made with the fœtal blood in veal-bouillon, and these proved that in some instances the blood of all fœtuses from the same mother contained bacilli; sometimes from the same litter all cultures remained sterile, while in some the blood of only one fœtus would yield a positive result. From these experiments the authors came to the conclusion that the tissues of the placenta offer no insurmountable obstacle to the passage of the bacillus of anthrax from the maternal into the fœtal circulation. Kowbassoff came to more positive results in his experiments. In all of his experiments the fœtuses of the infected animals contracted the disease *in utero*. He also found that time played an important rôle as far as the number of bacilli in the fœtus was concerned, as the longer the period which intervened between the inoculation and the death of the mother, the more numerous were the bacilli in the fœtal organs, showing that the migration of microbes from the maternal to the fœtal side of the placenta is continuous. Inoculation with attenuated virus proved that intra-uterine transmission took place more slowly. Inoculation of gravid animals with a very strong culture nearly always proved fatal to the fœtuses. Manzeri believes that direct transmission of microbes from mother to fœtus through normal placental vessels is impossible. As the result of an extensive study of the literature of this subject and of original experiments, he has come to the conclusions that no formed elements naturally pass out of the mother's blood into the fœtal circulation. Cinnabar, Indian ink, carmine, and other finely-divided pigment materials were injected into the jugular veins of animals far advanced in pregnancy, but in no case could any trace of the substance employed be found in the fœtus. According to his views, passage of formed elements can only occur when the placenta becomes diseased by inflammation, or is partially detached so that the walls of the villi are destroyed. He maintains that only under these conditions can pathogenic micro-organisms be transmitted from the mother into the fœtal blood. Most all authors agree that when extravasations or other pathological processes occur in the placental attachment, the direct entrance of microbes from the maternal into the fœtal circulation is not only possible, but a probable occurrence. Abnormality of the placental circulation must, therefore, be recognized as a condition which favors the occurrence of hereditary microbic disease. *Both clinical observation and experimental research leave no room for doubt that in some infectious diseases, at least, heredity is traceable to direct transmission of the specific microbes, either by means of transportation by the spermatozoa to the ovum, or by their* *entrance through the thin wall which separates the maternal from the fœtal circulation.* It is no more difficult to explain the migration of microbes through such a thin septum than their transportation from one tissue to another, and from organ to organ in other parts of the body, more especially as the anatomical conditions for mural implantation in the placental vessels are most favorable for such an occurrence.

CHAPTER VI.

NECROSIS.

NECROSIS, gangrene, mortification, and sphacelus are terms used synonymously to indicate the death of a part. English and American writers have usually restricted the meaning of the word *necrosis* to death of bone, while the remaining terms were used to express the same condition affecting the soft tissues. Recently a sharp distinction has been made between necrosis and gangrene from an etiological stand-point, according to which necrosis is said to have taken place when the circulation and nutritive changes in a part have completely ceased to be followed by gangrene as soon as saprophytic bacteria invade it and give rise to putrefaction. Death of bone will never be described as gangrene, and the moist putrefactive form of gangrene of the soft tissues will, in all probability, be never designated by the term *necrosis*. Necrosis of bone takes place in the same manner and results from the same causes as gangrene of the soft parts, and on this account there does not appear to be sufficient reasons to apply different terms to identical processes occurring in different anatomical structures; and yet by long usage they have become so intimately associated with the anatomical character of the part affected that it is difficult, for the present at least, to drop either. In modern literature we speak of necrosis of the soft tissues when the dead structures do not undergo putrefaction; that is, when this process takes place in the internal organs not readily accessible to putrefactive bacteria. In its extent necrosis varies greatly; it may involve an entire limb, an entire organ, or may be limited to a single cell. As a physiological process it occurs everywhere in the tissues, being limited, however, to individual cells incident to the wear and tear of the body, the pulling down and building up of the tissues, the cells that are lost being replaced by the normal process of regeneration. A simple, numerically increased cell necrosis, without normal restitution, leads to atrophy,—necrosis atrophica. When all the cells of a part undergo death simultaneously, the circulation corresponding to the area of dead tissue is arrested completely, and with this absolute ischæmia, plasma circulation, and all functions are, of course, completely suspended,—a serious pathological condition. A total necrosis has occurred.

ETIOLOGY.

Necrosis is a condition, not a disease. As a symptom it represents a local condition which has been brought about by different causes. The most frequent causes of necrosis are the following:—

Inflammation.—Inflammation may produce necrosis in two different ways: 1. Exudation and transudation take place so rapidly that complete stasis is produced by the extra-vascular pressure. 2. The bacterial cause of the inflammation is present in such large quantities that the vitality of the tissue is destroyed directly from this cause. If during an acute inflammation the capillary walls undergo such serious alteration that within a few hours or days the connective-tissue spaces become so densely packed with the corpuscular elements of the blood that the plasma circulation is greatly impeded or completely arrested, the primary inflammatory product encroaches upon the capillary vessels to such an extent as to completely arrest the already sluggish circulation. If such a copious and rapidly-forming inflammatory exudate give rise to complete stasis over a considerable area, the extent of the resulting necrosis will correspond to the district deprived of the requisite blood-supply. The same bacteria which produce inflammation frequently, if present in sufficient quantities, also cause cell necrosis. Ogston maintains that the staphylococci invade the tissues in the form of dense, round masses, which advance like clouds of a dense vapor, and, coming in contact with the tissues, induce necrosis, the cells, nuclei, and intercellular substance being changed into a homogeneous, wax-like substance before purulent liquefaction occurs. On the other hand, the streptococci of suppuration invade the intercellular spaces, the nuclei of the cells remaining visible. Bonone found the staphylococcus pyogenes aureus in such metastatic and broncho-pneumonic foci which presented a gangrenous character. He maintains that the staphylococcus at first produces in the lungs a necrosis by its multiplication, and that suppurative inflammation follows later around the necrotic tissue. Putrefaction of the dead tissue develops in consequence of the entrance of saprophytic bacilli through the bronchial tubes. He verified these assertions by experiments. He obtained pure cultures of the yellow coccus from such pulmonary foci made by intra-parenchymatous pulmonary injections, and succeeded in producing artificially identical lesions in the lungs of animals. The same result was obtained by the intra-venous introduction of small particles of elder-pith impregnated with pure cultures of the yellow staphylococcus. The gangrenous foci produced by emboli contaminated with the yellow coccus presented a characteristic appearance. The centre of such foci, at an early stage, is composed of necrotic tissue and remnants of dead leucocytes. The dead tissue is surrounded by a granular zone, which is again inclosed by a hæmorrhagic zone, and beyond this an area of catarrhal pneumonia. The staphylococci occupy the central portion and from here invade the granular zone, where putrefactive bacteria are also found. The pus-microbes do not reach the hæmorrhagic zone, or the tissues the seat of catarrhal pneumonia. As Bonone was unable to produce gangrene of the lung, either by parenchymatous injections of other bacteria, as the *pneumococcus* or *mikrosporon septicum*, or by aseptic emboli of elder-pith, he naturally came to the conclusion that the gangrene resulted from the specific effect of the yellow coccus. He compares gangrene of the lung with furuncle of the skin from an etiological stand-point. There can be no doubt that the primary effect of pus-microbes, when brought in contact with living tissue, under certain circumstances, is to produce necrosis before sufficient time has elapsed for parenchymatous inflammation to become established. This occurs in gangrene of the lung, furuncles, carbuncles, and *endocarditis bacteritica staphylococcica.* In the ordinary connective-tissue abscess, however, the connective-tissue cell undergoes the ordinary inflammatory changes before they are converted into pus-corpuscles, and if gangrene occur it is owing as much to mechanical obstruction to the circulation caused by a copious exudate as to the local toxic effects of the pus-microbes and their ptomaines. This difference in the action of pus-microbes on the tissues depends largely upon the rapidity with which they multiply at the point of primary localization. If the microbes are rapidly reproduced the chemical substances which they produce in the tissues are present in such large quantities that they destroy the cell protoplasm, and cell necrosis takes place as the result of their primary action; if the microbes multiply with less rapidity their effect on the tissues is less severe, and parenchymatous inflammation is produced instead of necrosis. Bonone used large quantities of pus-microbes in his injections, and the infected emboli caused circulatory disturbances, which only could favor rapid reproduction at the point of primary localization. Passet and Lübbert repeated his experiments, but used more diluted cultures, and probably on this account they were never successful in producing gangrene of the lung, while they frequently observed the development of a pulmonary abscess. The centre of a furuncle, as well as a carbuncle, is occupied by a mass of dead connective tissue, which later becomes detached by suppurative inflammation. The connective tissue in these cases is killed by the bacterial cause of the suppurative inflammation, which, toward the periphery, appears to become mitigated so that, behind the suppurating zone, a wall of granulation tissue is established which limits further extension of the disease.

Specific Bacteria.—All bacteria which can produce an inflammation sufficiently severe to completely arrest circulation can become an indirect cause of necrosis. Among these can be included the pus-microbes and the bacillus of anthrax. The necrosis which occurs regularly almost in every case of anthrax is probably due to the intensity of the inflammation resulting from the presence of the anthrax bacillus, to secondary infection with pus-microbes, or to the combined effect of both microbes. The absence of necrosis in artificially-produced anthrax, when pus-microbes are excluded by the strictest antiseptic precautions, does not prove that the anthrax bacilli possess no necrotic effect on the tissues, as in such instances death follows so soon that not sufficient time intervenes between the inoculation and the death of the animal for the local inflammation to terminate in necrosis. Necrosis is, however, much more likely to occur if the anthracic infection is complicated by the presence of pus-microbes. It is well known that certain chemical substances have the power to produce cell necrosis independently of their action to excite inflammation. Digitoxin, a poisonous principle of digitalis, is one of these. The primary effect of this substance on the tissues is to produce cell necrosis. We should expect that some of the ptomaines possess similar properties. Orthmann made some very interesting experiments in this direction with pus-microbes. He inoculated both corneæ in rabbits by making a puncture with a needle infected with a pure culture of the streptococcus pyogenes. One of the eyes was irrigated for ten minutes with a warm physiological solution of salt, by using an apparatus constructed for this special purpose. In the eye not thus treated a suppurative keratitis was initiated by the leucocytes from the conjunctival sac reaching the infected field, while in the cornea treated by irrigation the streptococci invaded the vascular spaces, and, multiplying with great rapidity, produced by their accumulation dilatation of the spaces and necrosis of the fixed tissue-cells.

In most of these cases the central necrosis led to perforation of the cornea and complete destruction of the eye. As the corneal corpuscles in the necrotic area had lost their nuclei and the parenchyma cells showed no signs of inflammation, we cannot escape the conclusion that cell necrosis was induced by the direct action of the ptomaines, elaborated by the masses of streptococci in the vascular spaces. The most conclusive proof of the destructive effect of ptomaines on the tissues has been furnished by the great master and founder of modern bacteriology, Robert Koch. In his experiments on septicæmia in mice he found, besides bacilli, a micrococcus in the neighborhood of the place of injection. Of the numerous kinds of bacteria contained in the putrid fluid used for injection, only the fine bacilli upon which the induction of the septicæmia depended and the chain cocci found a suitable soil in the mouse, while all the rest perished. The chain coccus was never found in the blood, but only in the tissues at the seat of infection. He found it exceedingly difficult to isolate it from the bacillus. At last he succeeded in cultivating it in the field-mouse, which, as experiments proved, is immune to the bacillus of septicæmia. The chain coccus injected into the subcutaneous tissue of the ear of the field-mouse invaded the tissues slowly, causing paleness and death of the cells without extravasation. The microbe entered and plugged the capillary vessels, but never found its way into the general circulation. Examination of the specimens showed that progressive gangrene occurred in advance of the microbes, hence could have occurred only by the action of ptomaines diffused through the tissues ahead of the microbic invasion. Inflammation of the fixed tissue-cells occurred around the zone of gangrene, and all leucocytes which reached the infected field perished. If the same animal was inoculated at the root of the tail, gangrene occurred and spread in a central direction, and resulted in death on the third day. The microbe did not change in its morphology or pathogenic properties after passing through a series of inoculations. Both Ogston and Rosenbach are of

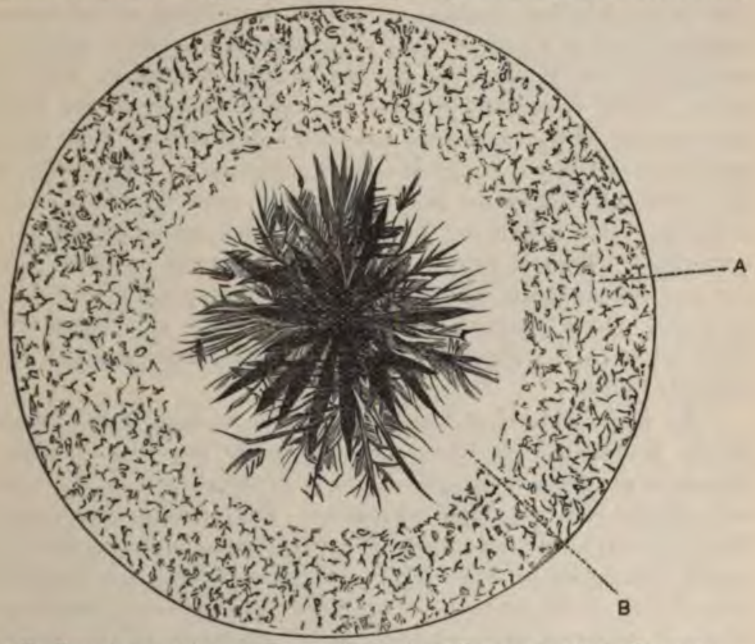

FIG. 48.—EXPERIMENTALLY-PRODUCED GROWTH OF STREPTOCOCCI IN CENTRE OF CORNEA OF RABBIT. HORIZONTAL SECTION, × 40. (*Baumgarten.*)

A, normal cornea; B, central necrotic portion, corresponding in outline to the star-shaped streptococci culture.

the opinion that the chain micrococcus with which Koch produced progressive gangrene in the field-mouse is identical with the streptococcus pyogenes. This question will have to be decided by future research, which must have for its object the isolation and cultivation of the chain coccus from the necrosed tissues of the field-mouse. Baumgarten is of the opinion that microbes can produce necrosis not only by the production of a tissue poison, but also by causing decomposition and by the assimilation of material necessary for cell nutrition. The explanation advanced by Koch ten years ago, however, appears more rational: "Introduced by inoculation (chain cocci) into living animal tissues, they multiply, and as a part of their vegetative process they excrete soluble substances which get into the surrounding tissues by diffusion, and when greatly concentrated, as in the neighborhood of the micrococci, this product of the organisms has such a deleterious action on the cells that these perish and finally disappear completely. At a greater distance from the micrococci the poison becomes more diluted and acts less intensely, only producing inflammation and accumulation of lymph-corpuscles. Thus it happens that the micrococci are always found in the gangrenous tissue, and that in extending they are preceded by a wall of nuclei which constantly melts down on the side directed toward them, while on the opposite side it is as constantly renewed by lymph deposited afresh."

An almost identical form of gangrene, as experimentally produced in the field-mouse by Koch, is occasionally met with in man. It is known as progressive gangrene, and is so called from its most conspicuous clinical feature—rapid extension. Before antiseptic surgery was known it frequently developed in cases of compound fracture and compound dislocation of large joints, and often proved the direct cause of loss of limb or life, or both. Two cases came under my own observation where it occurred after extirpation of carcinoma of the breast, in one without, and in the other with, removal of the axillary glands. In both cases the first symptoms appeared on the third day. The general symptoms were those of intense sepsis, while the local conditions resembled first what used to be called phlegmonous erysipelas. An erysipelatous blush appeared at the margins of the wound and extended rapidly in all directions, accompanied by infiltration of the deep tissues. The gangrene attacked the tissues first involved and followed the course of the phlegmonous inflammation. In spite of the most energetic local and general treatment, both patients died at the end of the first week. Rosenbach describes two cases that came under his care. In one the disease started from a small wound of a finger, the process finally extending to the lower extremities, with death on the sixth day. In the second case, the local lesion appeared first as a red induration, around which œdema developed rapidly, the skin covering the part presenting a reddish-blue discoloration before gangrene set in. This patient had an eruption of the skin over the whole surface of the body which resembled the rash of scarlatina. From the lesions of both of these cases Rosenbach cultivated upon peptone-meat gelatin the streptococcus pyogenes. Ogston calls this affection erysipelatoid-wound gangrene, and always found in the gangrenous tissue the streptococcus. Gangrene produced by staphylococcus, the same author calls sloughing inflammation or inflammatory mortification. The streptococcus of erysipelas never produces gangrene, and when this complication occurs in this disease it is always a positive indication that secondary infection with pus-microbes has taken place.

Putrefactive Bacteria.—Necrosis occurring from the action of any other microbes than those of putrefaction is not attended by any disagreeable odor or other evidences of putrefaction, and, if limited in extent and protected against the invasion of saprophytes, the dead tissue may be completely removed by absorption. Putrefactive bacteria feed on dead tissue, and in the absence of such they are comparatively harmless. Putrefaction only takes place in moist gangrene, and is always caused by the invasion of dead tissue with one or more species of saprophytes. Progressive gangrene, complicated by secondary infection with saprophytes, is characterized by the formation of gases which give rise to emphysema. Progressive gangrene with emphysema is one of the most fatal of all wound complications, as the ptomaines elaborated by the saprophytic bacilli greatly increase the danger from sepsis. Sulphuretted hydrogen is one of the gases formed during putrefaction of necrosed tissue. Rosenbach cultivated from the infected tissues, in 2 cases of progressive gangrene with emphysema, a saprophytic bacillus with spores. Hauser cultivated from putrefying organic substances one or more kinds of the *proteus*, the *proteus mirabilis* (*Zenkeri*) and *vulgaris*.

Trauma.—The vitality of a part is completely destroyed if a trauma is sufficient in intensity to arrest the circulation completely, and of such a character and extent as to render a return of it impossible. Such injuries, for instance, are caused by the passage of a car-wheel over a limb, where the skin often remains intact, while all of the deeper tissues are completely crushed. A blow against a part of the body where only a thin layer of tissue is interposed between the skin and an underlying bone may crush the subcutaneous tissue to such an extent as to preclude the possibility of a return of an adequate circulation, and necrosis follows as an inevitable result. Deep-seated contusions from the application of external violence are often attended by circulatory disturbances, which necessarily result in necrosis. Necrosis of ganglion-cells following contusion of the brain affords a good illustration of the occurrence of traumatic necrosis at a distance from where the force was applied. In such cases the cells are separated from all their anatomical connections by the trauma, and either undergo calcification or are removed by absorption. If such a contused area become the seat of a subsequent infection, suppuration or putrefaction can occur, according to the location of the part injured, infection taking place with pyogenic microbes or saprophytes. In the so-called railway-spine the cell necrosis following a contusion of the spinal cord leads to remote, central, and peripheral disturbances. A trauma may be of such a nature as to inflict an injury not incompatible with the integrity of a limb, but may create conditions which subsequently result in complete obliteration of a main artery. If an artery is subjected to serious pressure or traction, the intima gives way and its lumen is subsequently obliterated by the formation of a thrombus at the seat of injury. In such a case the artery is at first permeable, and the distal pulsations are unaffected until the lumen of the vessel is narrowed and finally completely obliterated by the formation of a thrombus. Professor von Wahl has called attention to an early and important symptom in these cases, the detection of which enables the surgeon to recognize the vessel injury before the appearance of the positive peripheral symptoms, viz., a *bruit*, which can be heard by placing the stethoscope over the seat of injury. The vessel injury in such cases is of serious import, as the contusion of the soft tissues which is usually also present retards or prevents the formation of an adequate collateral circulation, and gangrene occurs in consequence of complete interruption of the arterial circulation. A vein may be injured in a similar manner, and the venous stasis following obliteration by a thrombus may become a determining cause of gangrene of a limb, the vitality of which has been otherwise impaired by the injury.

Decubitus.—Prolonged uninterrupted pressure causes necrosis by interrupting the circulation. Tight bandaging and pressure of splints have often been productive of gangrene. Bed-sores are liable to form in patients suffering from acute infectious diseases, and in persons suffering from fracture of the spine, or disease of the spinal cord; also, in aged obese persons treated in the recumbent dorsal position for fracture of the neck of the femur. Decubitus is most prone to appear in consequence of pressure over bony prominences, and on this account we look for it in persons who are going through a long-enforced confinement in bed, first over the sacrum, the trochanteric regions, the spinous processes of the vertebræ, and the heels, parts most affected by the dorsal decubitus. The deleterious effect of pressure is greatly aggravated by filthy surroundings, as under these circumstances the necrosed tissue becomes the seat of infection with pus-microbes and saprophytic bacteria, which inaugurate a progressive gangrene and sepsis, often constituting the direct cause of death. It is not unusual, in cases of septic decubitus, to find the whole sacrum exposed, and in one instance that came under the author's observation the spinal canal was opened and through the opening the cerebro-spinal fluid escaped, first clear, later purulent. This patient lived for several days after the cerebro-spinal fluid had commenced to escape, and before his death he presented symptoms which indicated that the meningitis had extended to the envelopes of the brain.

Defective Arterial Blood-Supply.—The aseptic ligature, combined with the antiseptic treatment of wounds, has been the means of greatly diminishing the frequency of gangrene after ligation of the principal arteries of a limb in their continuity. Gangrene usually occurred, not so much from the sudden interruption of the arterial blood-supply as from the septic inflammation following the operation, which interfered with the formation of a satisfactory collateral circulation.

Ligation of Arteries in their Continuity.—Statistics of a number of years ago show that gangrene has followed ligation of the subclavian in the outer third in 9 per cent. of the cases reported; external iliac, 15 per cent.; common femoral, 11 per cent. The results after ligation of these vessels have much improved since the introduction of the aseptic ligature. In a healthy person with normal blood-vessels there is but little danger of gangrene following the ligation of the principal arteries of a limb with an aseptic ligature under antiseptic precautions. Gradual obliteration of an artery by a thrombus is not attended by equal danger of the occurrence of gangrene as when the same vessel is suddenly and completely blocked by impaction from the arrest of an embolus, because circulation is on a fair way of becoming established before the lumen of the vessel is completely closed, while in the latter case the demand on the collateral vessels is more urgent and sudden, and consequently the failure on their part to act as substitutes for the obliterated trunk is more frequent. Valvular disease of the heart, fatty degeneration of this organ, atheroma of the arteries,—in fact, all pathological conditions which diminish the *vis a tergo* are instrumental in the causation of gangrene, when from any accidental cause or operative interference the blood-supply to a limb has been diminished, or when the tissues are the seat of a progressive septic inflammation. Gradual diminution of the arterial blood-supply generally gives rise to dry gangrene, as is the case in senile gangrene, while sudden interruption of the circulation through a large artery from the application of a ligature or the impaction of an embolus is usually followed by moist gangrene.

Obstructed Venous Circulation.—Impeded venous circulation is fraught with as much danger, as far as the production of gangrene is concerned, as obstruction of the arterial circulation. Langenbeck was impressed with this fact so strongly that he recommended, if it became necessary to ligate one of the principal veins of an extremity near the trunk, to ligate at the same time the accompanying artery in order to guard against the evil results following ligation of a large vessel. Antiseptic surgery has minimized the danger of ligaturing, for instance, the axillary or femoral vein, and no surgeon at the present time would deem it necessary, or even justifiable, to ligate the corresponding arteries simply for the purpose of preventing excessive venous engorgement and of favoring the formation of an adequate venous collateral circulation. The same advantages which have resulted from antiseptic operations for the timely formation of an arterial collateral circulation after ligature of an artery are secured for the maintenance of an inadequate venous circulation after the ligation of a vein. Venous obstruction from pathological causes often proves more disastrous, as the causes which have brought about the formation of a thrombus frequently do not remain local, and the thrombus increases in length in both directions, thus rendering the formation of a collateral circulation a difficult, if not an impossible, occurrence. As venous obstruction gives rise to œdema gangrene, if it occur under these conditions, it always represents the moist variety, and is usually accompanied by putrefaction.

Heat.—Heat produces pathological conditions according to the degree of the temperature and the length of time a part is exposed to its action. A momentary exposure even to a high temperature produces only a burn of the first degree; that is, simply an active hyperæmia and redness of the surface. If the part is exposed for a somewhat longer time the hyperæmia is followed by a superficial inflammation and blisters form,—a condition which is described as a burn of the second degree. In such cases the necrosis is limited to the epidermis, which is detached from the papillary layer. In burns of the third degree the deeper tissues are destroyed by the heat, and extensive necrosis is the result. Cohnheim determined that a temperature from 54° to 58° C. was sufficient to produce gangrene in the rabbit's ear. If he immersed the ear for a short time in water heated to this temperature, necrosis always followed. A somewhat lower temperature continued for a longer time produced the same effect. Heat produces necrosis by coagulating the cell-protoplasm, if its action is superficial; if it penetrate more deeply, the blood in the blood-vessels is coagulated, and necrosis of the tissues deprived of circulation in this manner follows as an inevitable result. Intestinal ulceration, in case of extensive burns, is also a necrotic process, caused by capillary obstruction with dead or dying blood-corpuscles derived from the burned district. It has been found experimentally that a temperature over 45° C. has a destructive effect on the blood-corpuscles. Welti ascertained that if the ear of a rabbit is kept immersed in water, gradually heated to 70° C., bleeding from the nose and hæmoglobinurea followed,—symptoms which he attributed to partial or complete obstruction of capillary vessels with the third corpuscle of the blood.

Cold.—The action of cold in producing necrosis is closely allied to that of heat. Frost-bites are classified the same as burns. Cold, like heat, causes gangrene by producing by its action cell necrosis and vascular obstruction.

Cohnheim produced gangrene of the rabbit's ear by exposing it for a short time to a temperature of 16° C. The length of time a part is exposed, either to heat or cold, exerts an important influence in determining the extent and depth of the subsequent gangrene. Gangrene resulting from a burn or exposure to cold remains dry and aseptic as long as the entrance from without of pus-microbes and saprophytes is prevented, but with microbic invasion suppuration and putrefaction are established.

Caustics.—Chemical substances which by their local action on the tissues produce extensive cell necrosis are called caustics. Of these the strong acids and mineral salts destroy cells by causing coagulation. The necrosed tissue, or eschar, resulting from their action is firm, and the contour of the cells is well preserved. The alkaline caustics, on the other hand, dissolve the tissue elements, and the slough resulting from their application is soft. A peculiar form of necrosis of the maxillary bones occurs in persons exposed to the fumes of phosphorus. The most recent explanation of the occurrence of necrosis of the jaws in persons employed in match-factories is to the effect that the phosphorus fumes in the mouth are transformed into phosphoric acid, and that necrosis of the bone is produced by the direct action of the acid on the bone and myeloid cells, while the periosteum remains intact and produces new bone.

Ergot.—The prolonged administration of ergot in large doses is attended by the risk of causing gangrene. The gangrene from ergotism is always of the dry variety. It is generally believed that it is caused by the drug keeping up an angio-spasm, which shuts off the full blood-supply to the peripheral portion of the extremities,—the most frequent seat of the gangrene. Zweifel, of Erlangen, believes that the toxic effect of ergot results in a vasomotor paresis, and that the gangrene is due to defective innervation.

SYMPTOMS.

Internal Necrosis.—In simple cell necrosis the tissue elements may have undergone no changes in form, but the cell-protoplasm has lost its vital properties, and function has been completely arrested. Such cells present a cloudy appearance, and if the necrosis has resulted from a gradual or sudden ischæmia the part affected presents a pale appearance. In the periphery of such a necrotic area the vessels become dilated and a hyperæmic zone forms, in which the collateral circulation is to be established. If an artery in any of the internal organs is suddenly obliterated by the impaction of an embolus, the tissues supplied by the closed vessels are deprived for a time, and perhaps permanently, of their blood-supply, and in consequence of this they become pale, while around the wedge-shaped, anæmic territory the vessels concerned in the formation of collateral circulation are distended to their utmost, and often yield to the increased intra-vascular pressure when extravasation of blood occurs. If the collateral circulation is not speedily established, necrosis of the tissues supplied by the obliterated vessel is the result. In mycotic cell necrosis *karyolysis*—that is, dissolution of the cells—usually occurs. If the cell-membrane rupture and the contents of the cell escape, we speak of a *karyorhexis*. Absolute ischæmia of certain parts or cell territories continued for only one to two hours is sure to result in necrosis. If any portion of the brain, intestines, or kidney is deprived of blood-supply for this period of time, nutrition is completely suspended, and cell necrosis follows as an inevitable consequence. Litten ligated the renal artery in animals, and found, at the end of an hour and a half to two hours, the renal epithelia in a state of necrosis. Limited necrosis of the parenchyma of the brain may give rise to focal symptoms by which the lesion can not only be recognized, but often accurately located. Infarcts of the kidney can frequently be diagnosticated by a careful chemical and microscopical examination of the urine. A similar condition in the lungs gives rise to circumscribed catarrhal pneumonia, which can be recognized by a careful physical examination of the chest. Ulcer of the stomach, the result of a circumscribed necrosis, is attended by a complexus of symptoms pointing directly to the seat and nature of the lesion. Necrosis in internal organs is seldom followed by putrefaction, as saprophytes seldom reach the dead tissue. Necrosis of the lungs is sometimes followed by gangrene, by the entrance into the necrosed tissue of putrefactive bacteria from the respiratory passage.

Gangrene of External Parts.—As it is often impossible to recognize during life a limited cell necrosis in the internal organs by the symptoms presented, this subject has been briefly disposed of, but the symptomatology of external gangrene will receive a more thorough consideration.

It might appear that the recognition of the existence of gangrene of any of the external parts would require no special care or erudition. But this is not so. It is true that when gangrene is fully developed, when all the characteristic symptoms are present, a correct diagnosis can be made on first sight. But cases occur where it is exceedingly difficult to determine whether the part affected is dead or only in a state of inflammation. In illustration of this the author will only allude to the difficulties which surround the surgeon in many cases of herniotomy, when he has to determine whether it is justifiable to return a portion of intestine that has been strangulated for some time if he simply relies on the appearance of the intestine. The intestine presents a dusky, almost black appearance, and the casual observer might come to the conclusion that it is gangrenous, and treat it as such, when, in fact, a more careful observation will soon reveal the fact that the circulation is not completely arrested, and that it is safe to return it.

(a) **Pain.**—Sudden, severe, often excruciating pain in a limb is the first indication which announces the occurrence of embolism in one of the large arteries. In the lower extremity the embolus is often arrested at the bifurcation of the popliteal artery, but the pain extends along the whole limb, from the toes to the groin. The sudden anæmia is the cause of the pain. In senile gangrene the gradual ischæmia caused by the atheromatous degeneration of the arteries gives rise to pain and a sensation of numbness, which precede the gangrene for weeks or months. Acute inflammation resulting in gangrene is attended by intense pain from the very beginning; the pain abates, as a rule, with the occurrence of gangrene. Pain may be absent at the seat of necrosis, and referred to some other part or locality. In strangulated hernia the patient often suffers little or no pain at all in the swelling, but complains of a periodical pain in the region of the umbilicus. The absence of pain and tenderness over the region of a hernia speaks rather for than against the presence of gangrene. Osteomyelitis is attended by severe pain, which is diminished or subsides with the escape of the products of inflammation from the bone into the surrounding tissues. In cases of intestinal obstruction the cessation of pain, with continuance of the symptoms of obstruction, is an indication that gangrene has occurred.

(b) **Tenderness.**—The pain elicited by pressure is a more important symptom in the diagnosis of necrosis than spontaneous pain. As long as the part suspected to be necrotic is sensitive to the touch it is a sign that necrosis has not taken place. To test the sensation of a part it is advisable to resort to puncture with an aseptic needle. Absence of pain and all sensation on puncturing the tissues with a needle is often the best argument to convince the patient and friends that necrosis has occurred.

(c) **Temperature.**—The difference in the temperature of a part threatened with gangrene has given rise to the expressions *hot* and *cold* gangrene. If gangrene follow an acute inflammation, the local temperature remains high until other evidences of gangrene make their appearance, when the complete arrest of circulation and tissue metamorphosis result in a sudden fall of the local temperature. In gangrene following atheroma, thrombosis, embolism, and ligation of arteries the local temperature is reduced before gangrene occurs.

(d) **Pulse.**—After ligation of the principal artery of a limb the surgeon examines anxiously from day to day for the appearance of pulsation in the distal portion of the artery,—an occurrence upon which depends the fate of the limb. The re-appearance of the pulsation in the distal part of the artery is a certain indication that collateral circulation has become established, and that gangrene will not occur. With the appearance of distal pulsations the local temperature increases, and the diminished tissue metamorphosis is restored to its normal state. In embolism or thrombosis of a large artery, the same disturbances in the peripheral circulation of the limb are observed as after ligation. By searching for pulsation in different parts of the limb the surgeon can often locate the thrombus or embolus. If, for instance, the embolus or thrombus is located in the terminal portion of the popliteal artery, pulsations of the femoral artery can be felt from Poupart's ligament down to the seat of obstruction, while no pulsations below this point can be felt until collateral circulation is established. Obliteration of an artery from pathological causes is prone to prevent the formation of an adequate collateral circulation by the growth, in both directions, of the thrombus or embolus. The pulse furnishes the most important means to follow from day to day the growth of the intra-vascular blood-clot. In senile gangrene a thrombus frequently forms in one of the smallest arteries and grows in a proximal direction, extending from the digital branches to the dorsalis pedis, to the anterior tibial, or from the plantar arteries to the posterior tibial, the popliteal, and finally the femoral. In such cases the arteries can be felt as firm cords, but pulsations are limited to the previous portion of the vessels. An embolus often becomes the centre of an enormous thrombus, which seriously impairs the chances of preservation of the limb by the establishment of an early and adequate collateral circulation. If an embolus obstruct the popliteal artery, pulsations can be felt above this point, but they disappear with the extension of the secondary thrombus in a proximal direction.

(e) **Swelling.**—In moist gangrene the necrosed tissue imbibes moisture to a considerable extent, and the slough is larger than the tissue it represents. The swelling is twice more increased if gas forms in the tissues. In dry gangrene the parts shrink, become firmer, and instead of swelling there is diminution in their size as compared with their volume in a normal condition.

(f) **Emphysema.**—The presence of emphysema in gangrenous tissue is a certain indication of the presence of gasogenic bacteria. The character of putrefaction depends on the kind of saprophytes which are present in the dead tissues. The different kinds of *proteus* possess gas-producing properties. The *proteus*, according to Hauser, appears in different forms, according to the chemical reaction of the soil upon which it grows. On acid gelatin the culture consists of cocci and short bacilli; on alkaline gelatin it grows in the form of threads, vibrios, spirilli, etc. All these different forms of proteus growing in dead tissue exposed to the atmospheric air produce sulphuretted hydrogen. Hauser cultivated the proteus from ulcerating carcinomas and bed-sores. In the cases of progressive gangrene with emphysema examined bacteriologically by Rosenbach, he found the bacillus saprogenes. Emphysema is sometimes so marked that on percussion a tympanitic resonance is elicited. When less in degree its presence can be readily recognized by pressure, which causes a crackling, crepitating sound.

(g) **Color.**—If gangrene take place in consequence of interrupted arterial circulation, the part at first presents a preternaturally pale appearance until the first visible evidences of the actual occurrence of gangrene are announced by a livid or lead color, at a point where the circulation has first been completely arrested. The lividity, when it is due to complete, irreparable capillary stasis, is not affected by pressure. Blisters containing a sanious fluid form at points where the deeper tissues have already undergone necrosis. As soon as the circulation has been completely arrested, tissue metamorphosis is at once suspended, and the further changes are entirely of a chemical nature. The colored corpuscles of the blood undergo rapid disintegration; the coloring material is diffused through the dead tissue and into the interior of the bullæ. The black color of gangrenous tissue is produced by sulphuret of iron,—a combination of sulphuretted hydrogen and hæmoglobin.

(h) **Condition of Tissues.**—The condition of the dead tissues will depend on the cause of the necrosis. In dry gangrene they become firmer by evaporation of the fluids. In moist gangrene they imbibe fluids and undergo maceration, becoming soft and friable. A fetid, sanious fluid escapes from the dead tissue. Adipose tissue in a condition of gangrene undergoes speedy disintegration, and free globules of fat are mixed with the sanious discharge. Maceration of tissue is considered by Ravoth as the most important condition in determining the presence of gangrene in cases of strangulated hernia. He maintains that if the tissues of the intestinal wall can be readily separated and teased asunder with a dissecting forceps there can be no doubt that gangrene has occurred. This maceration, however, takes place only some time after the circulation has ceased, and is entirely absent in necrosis of bone, cartilage, and tissues well supplied with elastic elements, as the arteries. In determining the presence of gangrene in strangulated hernia, where any doubt as to its presence exists in the mind of the operator, it is much better to liberate the strangulated gut, draw it forward and irrigate it every few minutes with a hot solution of boracic acid, which will stimulate the sluggish circulation, and will soon furnish reliable proof of the actual condition of the vessels and the tissues. Mechanical stimulation of the intestinal wall is also a valuable diagnostic measure, as, if gangrene has occurred, no amount of irritation will excite peristaltic action, while with the restoration of the impeded circulation the muscular fibres will respond to irritation.

(i) Odor.—Necrosed tissue does not emit any unpleasant odor unless it has become invaded with putrefactive bacteria. The almost unbearable stench which attends extensive moist gangrene is always the result of putrefactive changes. Dry gangrene is odorless. In acute inflammatory affections of the lung, where a communication has been established between the inflammatory focus and the bronchial tubes, the presence or absence of fœtor is of great diagnostic value, as its presence speaks in favor of gangrene and its absence indicates an abscess.

(j) Mummification.—By this term we mean a drying up of a gangrenous soft part from the loss of fluids which it contains by evaporation. It is a state of preservation of dead tissue while still attached to the living body. It can only occur if the dead tissue is exposed to the atmospheric air, and on this account it is always absent in necrosis of internal organs. Mummification can only take place where putrefaction is absent, and, therefore, is most frequently met with where gangrene is first limited, and increases gradually by an aggregation of the causes which produce gradual diminutian of the arterial blood-supply, as in cases of senile gangrene.

(k) Line of Demarcation.—The line of demarcation is the line where the further extension of gangrene has been arrested by an adequate collateral circulation and a wall of living granulations. Back of this line of demarcation, on the side of the living tissues, there is to be found a hyperæmic zone, which precedes and attends the regenerative process, and by which the further extension of the gangrene is prevented. In septic gangrene the line of demarcation marks the limits of the area of infection, while in aseptic gangrene it indicates the point where the vascular conditions answer the physiological requirements of the part.

(l) Elimination of Gangrenous Part.—Spontaneous elimination of a gangrenous part is of frequent occurrence. The necrotic tissue may be disposed of in a spontaneous cure in three different ways: 1. Absorption of dead tissue. 2. Separation of necrosed part by granulation. 3. Separation of the sphacelus or sequestrum by suppuration. A limited quantity of necrosed aseptic tissue can be completely removed by absorption in the same manner as absorbable aseptic substances are removed when implanted in the tissues. This is the most desirable termination of gangrene, and takes place frequently in cell necrosis of the internal organs. Such a disposal of aseptic necrosed tissue is also possible on the surface of the skin when the area does not exceed a square inch, and an aseptic condition is secured throughout. The capacity of the tissues to remove aseptic necrosed tissue is limited, and when the quantity of tissue surpasses this capacity the dead part is considerably diminished in size, and the balance is detached by the granulations which form at the line of demarcation, and is finally eliminated spontaneously or by operation. Repair after this manner of elimination is rapid and satisfactory. If infection with pus-microbes has taken place in the beginning of the lesion which has caused the necrosis, or, later, at the line of demarcation, separation of the slough takes place by means of a suppurative inflammation. In such cases the dead part is not diminished in size, and the healing, after its elimination, takes place more slowly, and the result, as a rule, is less satisfactory. Separation takes place very slowly in necrosis of bones, intermuscular connective tissue, and tendons, requiring often weeks and months before the dead tissue can be removed.

(m) Liquefaction of Necrosed Tissue.—Where no putrefaction or suppuration takes place, and the amount of necrosed tissue exceeds the absorptive capacity of the surrounding tissues, liquefaction takes place, and months and years later the seat of necrosis is occupied by what appears, and has often been falsely described, as a cyst. This method of disposing of the dead tissue is observed most frequently in organs scantily supplied with connective tissue, as the brain and spinal cord and in adipose tissue.

(n) Encapsulation.—A limited area of aseptic necrosed tissue, not amenable to absorption, is often rendered harmless by encapsulation. The surrounding living tissue throws out a wall of granulation tissue which is converted into connective tissue, forming a capsule around the dead tissue. This method of disposal of dead tissue frequently occurs in the internal organs. A sequestrum occasionally becomes encapsulated after the interior of an involucrum has been rendered spontaneously, or by treatment, aseptic.

(o) General Symptoms.—These will have reference to the loss of function caused by cell necrosis in internal organs and sepsis in external necrosis. Function will be affected according to the location and extent of cell necrosis. If cell necrosis is of mycotic origin and general it frequently becomes a direct cause of death. If it is limited to a single organ the symptoms will point to it as the seat of the disease. Limited areas of cell necrosis, in most of the organs, may give rise to ill-defined or no symptoms whatever, and is then completely beyond the grasp of a correct diagnosis. The most important general symptoms of gangrene arise from the introduction into the general circulation from the gangrenous part of soluble toxic substances. As this subject will be treated of more extensively in the chapter on Septicæmia, it will suffice here to make the broad but correct statement that septicæmia complicates gangrene only when the dead tissues are infected with pus-microbes or putrefactive bacteria. Dry gangrene is, therefore, not attended by any danger of septic intoxication, while patients suffering from moist gangrene with putrefaction die, as a rule, not from the loss of tissue from gangrene, but from sepsis incident to the gangrene. Sepsis in gangrene is usually of that variety which arises from the introduction into the circulation of preformed toxines, the symptoms subsiding with the removal of the cause, with the exception of those cases of progressive sepsis caused by infection with pus-microbes.

CHAPTER VII.

NECROSIS (*continued*).

PATHOLOGICAL AND CLINICAL VARIETIES OF NECROSIS.

THE pathological and clinical classification of necrosis is based upon its causes, location, extent, and the age of the patient. The causes of necrosis have already been considered, and it has been shown that it results either from arrest of the circulation from purely mechanical causes or from the action upon the tissues of toxic, chemical, or thermal influences which destroy the protoplasm of the cells directly. The location of the necrosis is important to remember, as when it occurs in organs inaccessible to saprophytic micro-organisms putrefaction never takes place; on the other hand, necrosis in parts accessible to atmospheric air is prone to be followed by putrefaction, with all the dangers which attach themselves to this condition. The extent of the gangrene has an important bearing on the prognosis, as, when the causes are such as to determine a circumscribed form of the disease, life is not in danger, while the progressive form, with few exceptions, ends in death, in spite even of the most heroic treatment. The age of the patient often determines the form of gangrene, as, for instance, senile gangrene is a disease of the aged, while noma, almost without exception, attacks only children. The simplest and an exceedingly common form of necrosis is what has been described by Weigert as

Coagulation Necrosis.—This is essentially a cell necrosis. It is called coagulation necrosis because the tissues present the appearance of coagulated albumen, and also on account of the process resembling coagulation of the blood. Coagulation necrosis is probably identical with, or, at any rate, nearly allied to, the hyaline degeneration of Recklinghausen and fibrinous degeneration of E. Wagner. The chemical process which results in coagulation necrosis is as yet imperfectly understood. Weigert maintains that the cell-protoplasm and, perhaps, all albumen-containing substances are converted by it into a substance resembling fibrin. Macroscopically, tissues which have undergone this form of necrosis present a yellowish or whitish appearance, and are of variable consistence. Under the microscope the cells either appear unchanged in form or their place is occupied by thread-like fragments and granular material. Weigert lays down as the earliest change witnessed in a cell undergoing coagulation necrosis disappearance of the nucleus, which is the case twelve to twenty-four hours after the process commenced. Fibrin is a product of coagulation necrosis of the blood. According to Alexander Schmidt, during the coagulation of blood the colorless corpuscles disappear ; the product of their destruction is fibrin ferment and fibrino-plastic material, which, with the fibrinogen of the plasma, form fibrin. Isolated cells destroyed by coagulation necrosis exfoliate, and are transformed into a homogeneous granular substance, which, according to circumstances, is removed by absorption, or becomes encapsulated. Cell necrosis *en masse* is often followed by calcification, and on surfaces by ulceration. The transformation of a tubercular product into a cheesy mass is the result of coagulation necrosis. As essential conditions for coagulation necrosis to occur Weigert enumerates: 1. Death of tissue-cells. 2. Presence of plasma-fluids. 3. Tissues must contain coagulable substances. Coagulation necrosis is retarded by the ptomaines of pus-microbes, putrefying material, and living epithelial cells. An entire organ may be destroyed by coagulation necrosis. Pale infarcts after embolism are products of this change. The so-called fibrin wedges, which were formerly regarded as a decolorized blood-clot, consist of such tissues. At first the cells are normal in outline and appearance; later, the nuclei disappear and the cells break up into granular masses. In the internal organs coagulation necrosis is most frequently met with in the kidneys, spleen, typhoid deposits, tubercular lesions, the vicinity of mycotic foci, and in atheroma of the blood-vessels. In the parenchyma of organs it attacks the epithelial cells, while the connective tissue remains intact. On mucous surfaces it is represented by the diphtheritic and croupous exudations. *While the chemical processes which take place in coagulation necrosis cannot as yet be explained satisfactorily, there can be no doubt that this form of necrosis is nearly always, if not always, of mycotic origin, and it must be regarded practically in the light of a bacterial necrosis.* Klebs describes the same condition as *karyolysis*, *karyorhexis*, and *vacuolar degeneration*. He claims that early disappearance of the nucleus is not an essential, but an accidental, condition. In a case of pseudo-diphtheria Klebs found the bacilli between cells devoid of nuclei, and only in the centre of the necrotic patch did he find bacilli within the cells ; from this he concluded that karyolysis is due to the action of chemical products of the bacilli. In the second group of mycotic necroses the process differs as in typhus. Here the necrotic centre, which contains no cells, is surrounded by a zone, in which both cells and nuclei are also absent, but which contains a large number of chromatin bodies, lying free in the tissues. As these bodies are found in a location where the cells and nuclei have been destroyed, it can hardly be doubted that they represent remnants of these. According to Wolmkom and Grassle, these bodies are liberated by rupture of the nuclear envelope. This method of cell destruction is called *karyorhexis.* A third form of cell necrosis is *vacuolar degeneration*, in which the change is initiated in the protoplasm itself. This must not be mistaken for cell œdema. In vacuolar degeneration the protoplasm ruptures, and the nuclei of epithelial cells, which line a hollow viscus, are liberated, as Langhans observed in this form of cell necrosis in the kidney. The cell ruptures on account of increased intra-cellular pressure, and the process well deserves the name *plasma rhexis.* This form of cell destruction was formerly considered a post-mortem change. For the sake of simplicity it is advisable to substitute for the different forms of cell necrosis described by Klebs the general term, coagulation necrosis, devised by Weigert.

Necrobiosis.—This is a term applied by Virchow to the spontaneous wearing out of living parts. Death of isolated cells is a physiological process as long as they are replaced by new cells of the same tissue type. Necrobiosis occurring on a more extensive scale is a pathological condition, and is etiologically identical with coagulation necrosis. The term can be used to signify circumscribed cell necrosis without reference to its etiology or minute morbid anatomy.

Progressive Gangrene.—This form of gangrene is always of bacterial origin. The microbe most frequently found in the tissues is the streptococcus pyogenes. It occurs most frequently after wounds which open up a large surface of loose connective tissue, as in compound fractures, compound dislocations, excision of the breast, with removal of axillary glands and extirpation of large, fatty tumors. The streptococcus invades the connective-tissue spaces rapidly, somewhat after the manner of diffusion of the streptococcus through the lymphatic vessels. Much of the connective-tissue necrosis results from the direct action of the pus-microbes and its ptomaines on the cells. The necrosis of the skin is no indication of the extent of the disease in the deeper tissues. The infection is initiated by a chill, and the fever which follow resembles severe sepsis from other causes. If infection occur during the operation, or at the time of accident, the first symptoms may be looked for within forty-eight to seventy-two hours. If suppuration has occurred it is diminished with the appearance of septic infection, and the discharge becomes thinner and sanious. Lymphangitis frequently accompanies the deep-seated phlegmonous inflammation. Gangrene appears in the tissues first affected, and spreads rapidly along the connective tissue. Not only the gangrene is progressive, but also the attending septicæmia.

The larger the area of necrosis, the more extensive the field for the growth of pus-microbes and putrefactive bacteria. Progressive gangrene is an exceedingly dangerous form of infection, and unless treated by heroic measures at an early stage is sure to lead to a speedy fatal termination.

Progressive Gangrene, with Emphysema.—Etiologically this form of gangrene is identical with the preceding *plus secondary infection with gasogenic bacteria*. The necrosed tissue answers the purpose of a nutrient medium for saprophytic micro-organisms, which not only generate gas which is diffused through the dead tissues, but the soluble toxic substances which they elaborate in the necrotic area are absorbed into the circulation,—an occurrence which gives rise to toxæmia. Emphysema almost always extends far beyond the limits of the visible gangrene, but its presence is a sure indication of the extent of the infection in the deep-seated tissues. Progressive gangrene, with emphysema, is the most fatal form of gangrene, and only in exceptional cases will the surgeon succeed in warding off a certain fatal termination by early operative interference. In both kinds of progressive gangrene the part is swollen, œdematous, the skin presenting first a livid, bluish color, which afterward shades into a greenish or reddish-black hue. Bullæ, containing a reddish serum, form at points where the gangrene is spreading. Besides sulphuretted hydrogen, butyric and valerianic acid, ammonia sulphur, etc., are some of the many chemical products of putrefaction. The rapidity with which progressive gangrene, with and without emphysema, spreads, has led the French authors to apply to them the term *gangrene foudroyante*.

Moist Gangrene.—Progressive gangrene is necessarily a moist gangrene, as bacteria cannot germinate without moisture. All forms of mycotic gangrene are forms of moist gangrene. All necrosis in the interior of the body belong to this variety. The moisture of the dead tissue is due to imbibition of the œdema-fluid, and consequently moist gangrene is apt to follow vascular conditions, in which there is some impediment to the return of venous blood, as in cases of obstruction in a large artery, and more especially when a large vein has become obliterated by a thrombus. Moist gangrene is attended by all the dangers incident to putrefaction. In this form of gangrene the line of demarcation is the seat of suppurative inflammation.

Dry Gangrene.—In dry gangrene the dead tissue undergoes mummification, and on this account the soil is unfitted for the germination of putrefactive bacteria. Dry gangrene is usually the result of a trauma, the action of a chemical substance, or it follows a diminished blood-supply. In senile gangrene it follows in consequence of a gradual diminution of blood-supply, owing to atheromatous degeneration of the arteries, while the return of venous blood remains unimpaired. Dry gangrene is often an aseptic gangrene. If no infection take place with pus-microbes the line of demarcation is formed by granulation tissue, and the gangrenous part, if small, is absorbed, or if this is impossible on account of its size it is separated by the granulations. If suppuration take place this occurs at the junction of the dead with the living tissues. Dry gangrene is usually not attended by any general symptoms, and all attempts to remove the dead tissue should be postponed until the line of demarcation has formed.

Senile Gangrene.—This is the gangrene of the aged, or, rather, it is the gangrene which is caused by atheromatous degeneration of the arteries. Senile marasmus, in the form of atheromatous degeneration of the arteries, may occur in persons less than 40 years of age, and is often absent in octogenarians. Senile gangrene always occurs in parts where the circulation is feeblest; consequently it usually commences in one of the toes. If the necrosed tissue remain aseptic the rapidity of the extension of the gangrene depends on the condition of the blood-vessels. It may remain limited to one toe, or it may extend from toe to toe, and then creep along the dorsum or plantar surface of the foot, or on both sides simultaneously, and extend quite rapidly to the leg as far as the knee. Usually the disease extends along the course of one of the principal arteries, and extends later to other parts of the foot in consequence of greater embarrassment of the arterial and venous circulation. If infection in the vicinity of the necrosed tissue with pus-microbes take place, a suppurative inflammation may follow senile gangrene, which will give rise to a progressive and rapidly-fatal form of the disease. In the dry form of senile gangrene the tissues mummify, are firm, and perfectly black in color. In the moist variety the parts present the same appearances as in progressive gangrene. If a line of demarcation form, the separation of the dead from the living tissues requires an unusually long time, as the circulation is enfeebled to such an extent that tissue proliferation takes place very slowly.

Diabetic Gangrene.—It is a well-known clinical fact that persons suffering from diabetes are very prone to be attacked by gangrene. The reasons for this are as yet unknown. Gangrene occurring from trivial causes in persons presenting the appearances of usual health, and in whom no evidences of atheromatous degeneration of the arteries can be detected, should awaken the suspicion of the existence of diabetes, and no time should be lost in making a careful examination of the urine. A strictly antidiabetic diet has often resulted in arresting further extension of the gangrene. König has found that after amputation for gangrene in diabetics the quantity of sugar in the urine is diminished.

Decubitus.—*Gangræna per decubitum* literally means gangrene from pressure. It occurs in consequence of pressure from splints, bandages, and the prolonged recumbent position in bed, especially in persons suffering from fracture of the spine, or acute infectious diseases attended by great impairment of the circulation. Pressure without infection is productive of dry aseptic gangrene, but usually gangrene from this source is complicated by infection with pyogenic or putrefactive bacteria, or both. If gangrene from pressure is inevitable, it is apparent that its occurrence should be met by timely precautions for the purpose of preventing accidental infection. Gangrene from splint pressure can be prevented by interposing between the splint and bony prominences a thick cushion of salicylized cotton. Bed-sores should be prevented by changing the position of patient frequently and protecting the parts most exposed to the ill effects of pressure with fenestrated rubber cushions, by enforcing absolute cleanliness, and by keeping the skin in a healthy condition by applications of spirituous lotions. Both in *gangræna per decubitum* and senile gangrene the necrosis is caused by impairment or complete suspension of the capillary circulation.

Noma.—Noma, *cancer aquaticus*, is characterized by rapid, gangrenous destruction of the cheek, which usually commences some distance from the lips. This disease is exceedingly rare in this country, but quite prevalent in the large cities of Europe. It attacks exclusively children, occurring most frequently between the ages of 3 and 8 years. Healthy children seldom suffer from this disease; it either appears in badly-nourished, cachectic subjects, or it occurs as a complication of some of the eruptive fevers or typhus. In reference to the etiology of noma, little is known. The almost constant occurrence of the disease in a distinct part of the cheek and its limitation to one side of the face would indicate that it might be the result of some nervous disturbance. It is, however, more probable that it is a form of mycotic necrosis. A few observations on the bacterial origin of noma have been made. Lingard found in the tissues a long bacillus, which he believed was the cause of the disease. In gangrenous stomatitis in the calf, which affects this animal at particular seasons of the year, he found bacilli which are very similar in appearance to those present in noma in man. On cultivation they present characters which render them easily distinguishable from other bacteria, and on inoculation of these micro-organisms into the calf a gangrenous stomatitis is again produced.

Ranke's investigations on noma led to the following conclusions: Different forms of gangrene resulting from noma can unquestionably occur spontaneously in children who have a tendency to disease of this character; that is, without infection from contact. The frequent occurrence of noma in public institutions, and the apparent preference of the disease for localization upon the mucous membrane of the different openings of the body, suggest that the origin of it may be referred to the invasion from without of micro-organisms. In the zone of tissue contiguous to that which has undergone necrosis may be found cocci, which in number appear like a pure culture. At the periphery of the necrotic zone which has been invaded by cocci the connective tissue is found in a state of active proliferation. The entire condition is suggestive of the tissue necrosis in field-mice, which is caused by a chain coccus, described by Koch. Up to the present time the specific nature of the cocci which Ranke found in noma tissues has not been shown. Undoubtedly, further bacteriological research will prove that noma is a mycotic necrosis, and that the dead tissue, like in other forms of necrosis, is subsequently invaded with putrefactive bacilli. The disease commences as a circumscribed livid spot upon the surface of the mucous membrane of the mouth, and a corresponding portion of the cheek in its entirety is indurated. Soon the color of the affected mucous membrane becomes darker, and the skin, which at first presented a dusky appearance, is turned nearly black, and the epidermis is elevated in a blister, which afterward is turned into a black eschar. With the separation of the gangrenous part an opening in the cheek is left without any sign of a line of demarcation. The gangrene spreads in all directions, and, if not arrested spontaneously or by the use of energetic measures, often destroys the entire cheek. The disease is not limited to the soft tissues, but attacks the maxillary bones, often causing extensive necrosis and loss of teeth. The gangrene seldom extends beyond the median line in the lips, and the tongue usually remains free. In the majority of cases the disease is fatal. Death is preceded by symptoms of intense sepsis, with secondary septic inflammation of some of the internal organs, especially the intestines and lungs. In some cases a gangrenous affection of the genital organs occurs, which in every respect resembles the affection of the cheek. In case recovery takes place, the defect caused by the necrosis has to be restored by a plastic operation.

Hospital Gangrene.—*Gangræna nosocomialis*, *ulcerative-wound diphtheritis*, only occurs as an infection of wounds, and, as the name hospital gangrene indicates, is seldom met with outside of large unsanitary hospitals. Before wounds were treated antiseptically, it occurred as a frequent complication after operations or open injuries in most of the European hospitals. It was prevalent among the wounded during the War of the Rebellion. Thanks to the labors of Lister and his followers, it has now disappeared almost completely among civilized nations. The simple fact that this dreadful disease has been almost completely expunged from the oldest and most infected hospitals by the antiseptic treatment of wounds furnishes conclusive proof of its mycotic origin. Unfortunately, practical bacteriology was born too late to take advantage of the numerous opportunities to study the etiology of this form of wound infection. A feature of this disease of unusual bacteriological interest is the fact that it attacks not only recent wounds, but also wounds covered by healthy granulations. A healthy granulating surface is considered as a good, if not an absolute, protection against the ordinary pathogenic bacteria which infect wounds, but the microbe of hospital gangrene manifests no such discretion. The first evidence of the appearance of hospital gangrene is the formation of a yellowish, pultaceous mass upon the surface of a recent wound or upon a granulating surface. This mass can be readily wiped away, with the exception of the lowest layers, which are firmly attached to the surface. The skin in the immediate vicinity of this deposit becomes red and inflamed, and is soon displaced by the same material. The original wound assumes a yellowish-gray appearance, and is rapidly enlarged by the extension of the destructive process. Within three days to a week the wound is enlarged to double its original size. In this the *pulpous* form of the disease, extension toward the depth of the wound is slow, as fascia and muscles offer considerable resistance to its progress in this direction. In the *ulcerative* form of hospital gangrene the wound or granulation surface becomes the seat of an ichorous discharge, and the tissues undergo rapid destruction by molecular disintegration. The ulcerative form of hospital gangrene makes more rapid progress than the pulpous. Although these two forms occur as distinct affections throughout, combinations of the two have been observed. Hospital gangrene, in preference, attacks small wounds, as punctures, the bites of leeches, abrasions, blistered surfaces, etc. Many authors have been inclined to believe that diphtheritic inflammation of a wound and hospital gangrene are identical, but so far no positive proof of such identity has been furnished. The clinical course of both of these processes is nearly the same, but etiologically and pathologically the differences are apparent. Heine claimed that he observed hospital gangrene where the wounds were infected with virus from patients suffering from genuine diphtheria, and again he saw genuine diphtheritic lesions of mucous membranes in patients who were exposed to the contagium of hospital gangrene. The general symptoms in the beginning of an attack of hospital gangrene are not severe. The patient complains of a loss of appetite and a general feeling of malaise. In old persons, children, and debilitated subjects, it may prove fatal without the occurrence of special complications. One of the great dangers which attend hospital gangrene, especially the ulcerative form, is secondary hæmorrhage. During the pulpy degeneration or molecular disintegration of the tissues vessels are implicated, and a sudden hæmorrhage from a large vessel frequently leads to a rapidly fatal termination. The large vessels show an unusual resistance to the destructive effect of hospital gangrene, but not infrequently they give way, especially if the disease attack a stump after amputation. Septic intoxication is never so well marked in hospital gangrene as in diphtheritic affections of mucous membranes. Billroth believes that hospital gangrene is caused by a specific micro-organism which is only reproduced under certain atmospheric conditions; hence the appearance of the disease formerly in an epidemic form. Clinical observations leave no doubt that the disease is carried from one patient to another by means of sponges, instruments, hands, etc.

Perforating Ulcer of Stomach and Duodenum.—These ulcers follow circumscribed necrosis of the wall of the stomach or duodenum, caused by a diminished arterial blood-supply of a limited vascular district. That these ulcers are of vascular origin is shown by their shape and direct relation to an artery. The defect is in the form of a cone, the base being directed toward the lumen of the viscus, and the apex corresponds with a small artery which must have been partially or completely obstructed before the necrosis occurred. These ulcers are sometimes multiple, and in the stomach they are found in preference along the lesser curvature. After interruption of the arterial circulation the wedge-shaped ischæmic, necrosed portion is removed by the action of the gastric juice, and the ulcer is made. As perforating ulcer of the stomach or duodenum never occurs in cases of ulcerative endocarditis, but selects in preference young females, the causes of vascular obstruction must be of a local nature. The sphacelus shows molecular decay, but no trace of inflammation. Perforating ulcers of the stomach and intestines are of interest to the surgeon, because in case of perforation their treatment has been brought within the legitimate sphere of abdominal surgery. The more frequent occurrence of perforation is prevented by circumscribed plastic peritonitis, which seals the defect or establishes an adhesion between the affected portion of the organ and some other organ.

Perforating Ulcer of Foot.—This ulcer follows a localized necrosis of the foot, which is supposed to be in part, at least, the consequence of vasomotor disturbances, to which are added impediments to the circulation and frequently infection with pathogenic micro-organisms. This ulcer is remarkable for the regularity of its outline, looking as though a piece had been cut out with a punch. The defect corresponds to the shape of the detached necrosed tissue. The necrosis affects all of the tissues of the part in which it occurs, not even sparing the bones and articulations of the foot. The dissections of Duplay, Morat, Fischer, and others leave no doubt that this strange ulcer originates from necrosis following degeneration of the nerves of the affected region. Infection with pus-microbes follows the necrosis,—an occurrence which renders the treatment more intractable.

Ergotism.—One of the effects of chronic ergot intoxication is symmetrical dry gangrene. Bread made of flour containing ergot has not infrequently occasioned, in Europe, fatal epidemics, usually attended with dry gangrene. As before stated, the gangrene following the prolonged administration of [illegible] ither the result of a chronic angiospasm, or of a paraly[illegible] the drug on the peripheral nerves.

Prognosis.—The prognosi[illegible] a [illegible] of gangrene should be based on the etiology, location, and extent of the disease which caused the gangrene. The existence of complications must also be taken into careful consideration. Acute, rapidly-spreading gangrene, irrespective of the causes which may produce it, must always be considered as an exceedingly grave condition. Mycotic progressive gangrene, with and without emphysema, unless treated early and heroically, proves fatal almost without exception, death resulting from septicæmia. Gangrene following obliteration of the principal artery of a limb would result in death, in the majority of cases, unless a fatal sepsis is prevented by early amputation. Necrosis of the entire or greater part of important internal organs is incompatible with life from the greatly diminished or completely suspended function of important organs. The prognosis, so far as life is concerned, in cases of senile gangrene, is rendered exceedingly grave when the gangrene spreads rapidly, in consequence of an ascending arterial thrombosis, or thrombo-phlebitis, and life is in imminent danger when the gangrene due to diminished blood-supply is complicated by a rapidly-spreading suppurative inflammation, or if septic intoxication arise from invasion of the moist necrosed tissue with putrefactive bacteria. The general condition and age of the patient play an important part in arriving at correct prognostic conclusions. Patients debilitated from antecedent, acute, and chronic disease are in greater peril of life than robust, healthy persons whose circulation and tissue resistance has not been impaired. Infants and the aged succumb to gangrene more readily than young adults and persons in middle life, although the gangrene may have resulted from the same causes, reached the same extent, and inoculated the same parts. Gangrene of some important organ, as the lungs or intestines, is more dangerous to life than peripheral gangrene. The co-existence of complications, such as diabetes, Bright's disease, tuberculosis, valvular disease of the heart, and cirrhosis of the liver will influence the prognosis correspondingly.

Treatment.—The prophylactic treatment includes such measures, medicinal, dietetic, and otherwise, that are calculated to improve the blood-supply of the part threatened with gangrene, and if this has occurred, or is inevitable, to prevent putrefaction of the dead tissues. In threatened gangrene from obstruction of the main artery of a limb, the establishment of collateral circulation must be aided by placing the limb in a horizontal or slightly-elevated position, and by the external application of dry heat. In the aged suffering from premonitory peripheral symptoms of gangrene, its actual occurrence can often be postponed by massage, rubbing the limb from the toes toward the body for ten or fifteen minutes twice daily, and by the avoidance of all causes which would bring about stasis in the enfeebled blood-vessels. The minutest lesions of the skin, as abrasions, corns, bunions, ulcers, etc., should receive careful attention in all persons the subjects of a feeble circulation, as they frequently are the starting-point of a gangrenous inflammation. Diabetic persons are exceedingly liable to be attacked with gangrene after the slightest operation or the most insignificant injury, and on this account it is advisable to examine the urine before undertaking an operation in persons presenting the faintest evidences of this disease. As most forms of gangrene are of mycotic origin, all infective atria should be protected against infection from without by thorough antiseptic precautions. The prevention of decubitus has already been referred to, and here will be only mentioned the necessity of securing for the necrosed tissues an aseptic condition by rigid cleanliness and antiseptic measures in cases where the necrosis has occurred, or where it cannot be prevented. In moist gangrene the prevention of putrefaction is a most difficult task. Where gangrene of this type has occurred, or is anticipated, the whole surface far beyond the area involved or threatened should be rendered aseptic in the same manner as in the preparation for an operation, and the parts protected as far as possible against invasion with putrefactive bacteria by an absorbent antiseptic dressing. A few layers of gauze and a thick compress of salicylized cotton answer an excellent purpose in meeting this indication. If gangrene with putrefaction has occurred, the etiological indications for local treatment are best met by multiple incisions through the necrosed tissues and undermined skin and the application of a compress wrung out of a 1-per-cent. solution of acetate of aluminum. If the fœtor is intense, Labarraque's solution of chlorinated soda, properly diluted, answers an admirable purpose. In gangrene with partial separation of the slough and considerable undermining, permanent irrigation with either of these preparations answers the best purpose. All patients suffering from gangrene are debilitated from antecedent or concomitant causes, and consequently are badly affected by any form of the so-called antiphlogistic or sedative treatment. Fever is always the result of the entrance of septic material, and should therefore not be treated by antipyretics, but by local measures directed toward the primary cause. Quinine in sedative doses does more harm than good. Veratrum viride, tartar emetic, and the innumerable chemical substances which have recently been so much lauded as anti-fever remedies should never be prescribed in the treatment of fever attending necrosis. The patient's strength must be supported from the beginning by a liberal diet and the use of stimulants. If the heart's action is feeble, digitalis can be given with benefit. Quinine in tonic doses is indicated. Anorexia not dependent on high fever calls for some one or a combination of bitter tonics. The part affected must be placed at rest and in a position most favorable for the passage of the blood through the capillaries.

The question of removal of gangrenous tissue and the amputation of a gangrenous limb should receive thoughtful, conscientious consideration before an operation is undertaken. The favorable results which have followed the operative removal of a gangrenous part after the line of demarcation had formed, and the great mortality of operations undertaken without such a positive indication, have led many good surgeons to advise postponement of all operative procedure until nature has indicated the site of operation. This conservative rule, however, is incompatible with the teachings of modern surgery. We know that death in cases of rapidly-spreading gangrene is caused by septic intoxication. We also know that the cause of the septic intoxication inhabits the dead tissue, and we are also aware that the extension of the immediate cause of gangrene (vessel-obstruction), ascending thrombosis in the arteries, and ascending thrombo-phlebitis in the veins proceed from the gangrenous part. In view of these facts, the delay of operative measures in the treatment of gangrene until the line of demarcation has been established would be to wait for something which, in the most urgent cases, never occurs. In the absence of symptoms indicating danger from septicæmia it is not only advisable, but absolutely necessary, to postpone the operative removal of the gangrenous part until nature locates the site for the operation by the formation of the line of demarcation. In aseptic dry gangrene involving parts where no formal operation is necessary to secure a favorable healing, later spontaneous elimination should be waited for, and after separation of the necrosed tissue the granulating surface is treated in the usual manner. In moist gangrene the dead tissue is removed as soon as partial separation has taken place by dividing with scissors the more resistant structures, as fascia and tendons, after which the resulting wound is treated upon antiseptic principles. In gangrene of the extremities amputation can be done safely, and with good prospects of success, as soon as the line of demarcation has formed. In such cases it is necessary to remove as little as possible of the healthy tissue by carrying the incisions in such a manner as to leave flaps composed of healthy tissue simply long enough to cover the bone. No typical operation should be adopted, as the flaps must be made not in conformity with any text-book rules, but the condition of the limb. If the patient is febrile, and the character of the fever indicates as its origin the gangrenous part, delay, to say the least, is attended by increased danger of extension of the gangrene, and death from septicæmia. Such cases fare best at the hands of prudent but courageous surgeons. Procrastination in such cases is a sign of timidity or ignorance. What is to be done must be done at once. The patient and friends must be made acquainted with the dangers incident to delay, and the only prospect of recovery by early amputation. Consultation with one or more of the neighboring physicians is an absolute necessity in such cases. Fortified by a fair understanding with the patient and his friends, supported by the advice and counsel of one or more of his colleagues, no surgeon need fear to follow the dictates of his conscience, even in the most unpromising cases. The distinguished Hueter related several cases where early amputation saved the life of patients who were in stupor from the effects of septic intoxication to such an extent that an anæsthetic was unnecessary. Early amputation should be urged and done in all cases where life is placed in jeopardy from absorption of septic material from the gangrenous part. The results after amputation under such circumstances will always remain uncertain, because in many instances fatal general infection occurs soon after the development of the first general symptoms, and the local infection frequently extends to the site of operation, rendering a recurrence of gangrene in the stump a great probability. Amputation should be done, as near as possible, through healthy tissue. Much good judgment is necessary to determine this location. It is safe to maintain that the more acute the attack, the more distant should the amputation be made from the apparent boundary-line of the gangrene. In gangrene from obstruction of a large blood-vessel and in gangrene attended by ascending thrombo-phlebitis, arterial thrombosis, or both of these conditions, the line of amputation should fall through a point where the vessels are patent, otherwise a recurrence of the disease is almost sure to take place. Before the amputation is made the part to be removed should be enveloped in towels wrung out in an antiseptic solution for the purpose of preventing contamination of the wound with septic material from the dead tissue. It is almost needless to mention that Esmarch's elastic bandage should never be used, as by its application septic material might be forced into the circulation. The limb should be rendered as nearly as possible bloodless by holding it for a few minutes in a perpendicular position, when an elastic constrictor is applied some distance above the point selected for the amputation. In septic patients the parenchymatous oozing sometimes is difficult to control, but is managed most successfully by keeping the limb in the elevated position, and by making surface-pressure with a large, flat sponge or gauze compress wrung out in hot water. As most of these patients are prostrated from the effects of the disease, they are liable to suffer from shock, and measures should be resorted to to prevent this complication, or, at least, diminish its severity. For this purpose a subcutaneous injection of $\frac{1}{100}$ to $\frac{2}{100}$ grain of atropia with $\frac{1}{6}$ grain of morphia is administered hypodermatically before the anæsthetic is diminished. Two ounces of whisky or the same amount of brandy is given at the same time *per orem*, or, preferably, *per rectum*. Ether is preferable to chloroform in these cases as an anæsthetic. After the operation the most careful after-treatment is required to meet possible emergencies. Shock is treated by alcoholic stimulants, camphorated oil, musk, and coffee. If the stomach is irritable, brandy, whisky, or coffee is administered by the rectum. Camphorated oil or musk is given hypodermatically every half-hour until the patient reacts. External heat is useful in relieving congestions of internal organs and in stimulating the action of the heart. Amputation wounds made through tissues that are not positively known to be aseptic should always be drained; this is the more necessary if the soft tissues are œdematous. Should the tissues at the seat of amputation not present a satisfactory appearance, it is advisable to go up higher, more especially if the vessels are obstructed by a thrombus. The fate of the patient is decided within a few days after the amputation. The most favorable symptom is a reduction of the temperature to normal within a few hours after the operation, which will be the case if the fever has been caused by a septic intoxication. With the removal of the tissues which furnished the toxic substances and the elimination of these through the secretory organs the septic symptoms subside, and if the patient has sufficient strength left to carry him over the immediate effects of the operation the prospects of recovery are good. If the patient is the subject of a progressive sepsis, the amputation, in all probability, will prove powerless as a life-saving measure, as the microbes which have reached the circulation reproduce themselves with great rapidity, and death from this cause results within a few hours to several days. Prompt improvement soon after the operation, with recurrence of febrile symptoms in a few days, indicates the occurrence of gangrene in the stump. Such symptoms demand a change of dressing. If gangrene is present, all sutures are removed, a thorough local disinfection practiced, after which the stump should be treated by constant irrigation. Reamputation at this time would, in all probability, prove fatal, and reliance on local disinfection, combined with the use of stimulants and tonics, is advised, with a feeble hope that these measures may become the means of limiting the extension of the disease, and of supporting the heart's action until the line of demarcation is established, when the surgeon's services are again required to assist nature's efforts in the elimination of the dead tissues. In noma and hospital gangrene, the infected tissues are removed with the sharp spoon, and after thorough antiseptic irrigation the actual cautery is applied, and the further management of the wound is the same as in case of infected wounds from other causes. Chlorinated water or a solution of bromine are excellent preparations after the primary disinfection and cauterization in the treatment of these diseases.

CHAPTER VIII.

SUPPURATION.

BACTERIOLOGICAL CAUSES AND HISTOGENESIS OF SUPPURATION.

SUPPURATION is the most frequent termination of acute inflammation. Inflammation terminating in the formation of pus is called suppurative, both on account of its etiology and the nature of the inflammatory product. Suppuration is the process by which the morphological elements of the inflammatory product, the leucocytes, and embryonal cells are converted into pus-corpuscles. Suppurative inflammation is caused by the action upon the tissues of specific micro-organisms, the pus-microbes, and the transformation of leucocytes and embryonal cells into pus-corpuscles is accomplished by the same cause. The brilliant results which have been obtained by the antiseptic treatment of wounds made it exceedingly probable that all wound-infective diseases are caused by living micro-organisms. The probability was increased when Koch, in 1879, showed the direct connection existing between certain traumatic infective diseases in animals and the never-absent definite micro-organisms. It requires no longer any arguments to show, at this time, that all inflammatory wound complications, among them suppuration, are, without exception, caused by the introduction into the tissues of specific pathogenic microbes. Etiologically, most of the purulent processes constitute more of a unity than was formerly believed, and the clinical varieties are mostly determined by the intensity of the infection, the manner of localization, and the degree of resistance possessed by the tissues. The most conclusive evidence of the correctness of this assertion is furnished by the fact that the same streptococcus which produces a simple abscess is likewise the most frequent cause of progressive gangrene, and of that most grave form of suppuration—pyæmia.

I. HISTORY OF MICROBIC ORIGIN OF SUPPURATION.

As in the case of nearly all infective diseases, years before the specific pus-microbes were discovered, living organisms were found and described in pus, and were believed to be the essential cause of suppuration. Twenty-five years ago Klebs discovered, in the tubuli uriniferi in cases of pyelo-nephritis following suppurative cystitis, between the pus-cells, small, round cocci, which he believed produced the infection. In 1872 the same author published the result of his researches, during the Franco-Prussian war, on septic-wound diseases. In this work he again referred to the micro-organisms which he had previously described, and showed that they existed in the tissues and organs—the seat of suppurative inflammation—before pus had formed. He also showed how these micro-organisms enter the circulation and become the direct cause of pathological conditions in distant organs. Even at that time he placed great stress on the fact that, as long as the cocci remained only in the tissues at the point of infection, they produce only local inflammation or necrosis, but as soon as they enter the circulation fever and other symptoms of general septic infection follow.

Ogston, the discoverer of pus-microbes, published the results of his observations and researches in 1881. This patient investigator examined the pus of 69 abscesses for micro-organisms, and found in 17 of them a chain coccus (streptococcus), in 31 cocci which arranged themselves in groups which resemble a bunch of grapes (staphylococcus), and in 16 both of these forms were present. In cold abscess he was unable to find either of these micro-organisms. He also ascertained that these two forms of microbes differed in their manner of diffusion in and action on the tissues, as the streptococcus, following the lymph-channels and connective-tissue spaces, was seen to be the cause of diffuse suppurative processes, while the staphylococcus was found by him only in abscesses which were circumscribed.

Rosenbach took up the work where Ogston left it, and, as the fruit of a number of years of patient study and research, published his classical work in 1884 ("Microörganismen bei den Wundinfections Krankheiten des Meuschen," Wiesbaden, 1884). This work must serve as a basis for all future research on suppurative inflammation. Rosenbach availed himself of the advantages offered by an improved technique in bacteriological research, cultivated the different pus-microbes upon solid nutrient media, and pointed out the difference in the macroscopical appearances of the cultures of the different kinds of pus-microbes, which enabled him to differentiate between them by the naked-eye appearances of the cultures upon the different nutrient substances. He discovered the staphylococcus pyogenes aureus, the micrococcus pyogenes tenuis, and three kinds of bacillus saprogenes.

Passet should be mentioned next in the long list of distinguished names of original investigators who have made the bacteriology of suppuration a special study. He discovered and described the staphylococcus citreus and the staphylococcus cereus albus and flavus, and from a perirectal abscess he cultivated the bacillus pyogenes fœtidus. The streptococcus which he found he maintained was different from the one described by Rosenbach, as it resembled more closely the streptococcus of erysipelas, but this claim has not been substantiated by subsequent investigations. The bacillus pyocyaneus was described by Gessard and Charrin. The gonococcus, the specific microbe of gonorrhœa, was discovered by Neisser in 1879. In our own country the micro-organisms of pus have been studied by such men as Sternberg, Osler, Councilman, Ernst, and Park.

II. INDIRECT CAUSES OF SUPPURATION.

Inflammation produces in the tissues conditions which must be regarded as indirect causes of suppuration. These conditions favor the suppurative process by bringing the histological elements of the inflammatory product in a position or relation to the blood-vessels which impairs or suspends their nutrient supply. In acute inflammation the connective-tissue spaces become crowded, in a short time, with the corpuscular elements of the blood, which, by their presence in such great number, cause dilatation of these spaces and pressure upon the adjacent capillary vessels, which often result in complete stasis and consequently arrest of blood-supply. In consequence of suspended nutrition arising from vascular obstruction, the leucocytes undergo coagulation necrosis and lose their power of resistance to the action of pathogenic micro-organisms. If inflammation attack the fixed tissue-cells with an intensity short of producing necrosis, the cells proliferate and the embryonal cells thus produced constitute another source of histological elements of the inflammatory product. If the cells are produced in excess of the capacity of the inflamed part to supply them with new blood-vessels, the local anæmia thus created places them in the same unfavorable condition as the leucocytes in the crowded connective-tissue spaces, and they are exposed to the same risk of death from malnutrition. If, as the result of rapid tissue proliferation and local ischæmia, the embryonal cell become completely detached from the matrix which produced it, it is placed in the worst condition, so far as its vitality and vegetative capacities are concerned, and it readily succumbs to the deleterious action of the pus-microbes. It can be set down as a rule that all conditions, local or general, which impair cell nutrition favor the suppurative process. Suppuration in inflammatory foci is always observed first where cell nutrition is most impaired, hence in the primary inflammatory product among the leucocytes most distant from capillary vessels, and among embryonal cells that have become isolated or occupy a place most remote from the vascular supply.

III. DIRECT CAUSES OF SUPPURATION.

Clinical suppuration is caused by the action of pus-microbes on the leucocytes and embryonal cells, by which these cells, the morphological elements of the inflammatory product, are converted into pus-corpuscles. A number of investigators maintain that suppuration can be produced artificially in animals by injecting into the tissues certain

Chemical Pyogenic Substances.—The substances which have been found to possess the property of exciting suppurative inflammation are metallic mercury, turpentine, and croton-oil. Councilman introduced turpentine and croton-oil in aseptic glass capsules into the subcutaneous connective tissue of animals under strict antiseptic precautions, and, after the wound had healed and the capsules had become encysted, ruptured them subcutaneously. He found that both of these substances caused a circumscribed suppuration. Uskoff claimed that a considerable quantity of indifferent substances, such as milk, olive-oil, etc., if injected subcutaneously in animals, either at once or by repeating the injection from time to time, caused suppuration, and that turpentine administered in the same manner always acted as a pyogenic agent. Orthmann, under Rosenbach's supervision, repeated Uskoff's experiments, and, by resorting to more strict antiseptic precautions, could not verify the correctness of his conclusions in reference to the pus-producing properties of indifferent substances. His experiments with croton-oil, turpentine, and metallic mercury always resulted in inflammation and suppuration. Grawitz and de Bary ascertained that croton-oil, when injected in small quantities into the subcutaneous tissues of rabbits, caused a serous transudation or a fibrinous exudation, while larger doses acted as a caustic, and were only occasionally followed by suppuration. If they injected a mixture of pus-microbes and croton-oil it always was followed by the formation of pus. They maintained that certain chemical substances, used in a definite degree of concentration, injected into the subcutaneous tissues of animals, prepared the tissues for the growth of the pus-microbes. From a later series of experiments Grawitz became more firmly convinced that aseptic turpentine, used in sufficient quantities, always causes a suppurative inflammation in the connective tissue. Inoculations of different nutrient media with pus produced by turpentine showed that it contained no pus-microbes. He also determined that such chemical pus had a destructive effect on pus-microbes. This action of sterile pus he attributes not to the presence of ptomaines, but to the action of its albuminous constituents. His experiments also lead to the important observation that when gelatin cultures are over-saturated with albumen, or peptone, pus-microbes cease to multiply. Very recently Rosenbach has made a series of experiments which has convinced him that the chemical pyogenic substances which have been mentioned, when injected into the tissues of animals, cause suppuration independently of the presence of pus-microbes. Among those who, from their own experimental work, have come to diametrically opposite conclusions, can be mentioned Scheuerlen, Ruigs, Nathan, and Biondi. If we consider for a moment how difficult it is, in experimenting on animals with indifferent substances and chemical irritants, to procure for the seat of injection a perfectly aseptic condition, it is not difficult to conceive that opinions still differ in regard to the immediate and essential cause of suppuration. Taking it for granted that certain chemical pyogenic substances, when injected in sufficient quantities into the tissues of animals, have the power to produce suppuration, inflammation and suppuration produced in such a manner represent clinically suppurative affections. Neither the inflammation nor the suppuration following it are progressive in their character. The chemical substance produces inflammation over an area which corresponds with the extent of its diffusion, and the cellular elements of the inflammatory product are converted into pus-corpuscles by the destructive action of the substance or their protoplasm. The whole course of the artificial affection remains aseptic throughout, and the pus which is produced is aseptic and sterile, —not clinical, but chemical, pus. In suppuration, as we observe it at the bedside, the direct cause which produced it multiplies in the tissues, hence its tendency to become progressive, and from the pus which is produced the immediate and essential cause—the pus-microbes—can be cultivated. Practically, in man, the occurrence of suppuration from the action of pyogenic chemical substances would be possible only on the surface of the body.

Pus-Microbes.—That the pus-microbes are *the immediate and essential cause of suppurative inflammation and pus formation has been well established by clinical observation and experimentation.* Clinical experience during the last twenty years has shown beyond all doubt that suppuration in wounds can be prevented by measures which are calculated to remove, destroy, and exclude pathogenic micro-organisms from without. Rosenbach found that in dogs and rabbits a small quantity of a pure culture of the staphylococcus pyogenes aureus injected under the skin produced a most violent suppurative inflammation; cultures of the staphylococcus pyogenes albus had the same effect. Cultures of the streptococcus pyogenes produced only slight inflammation in rabbits, while they proved very fatal in mice. Passet took a pure culture of the staphylococcus pyogenes aureus the size of a pea, grown upon potato, and mixed it with 1 cubic centimetre of distilled water. Of this mixtur he injected under the skin of a mouse 0.1 cubic centimetre; the anim recovered. Another mouse was treated in the same manner, but 0.04 cubic centimetre of a liquefied-gelatin culture was used, and this animal died in eighteen hours. Cocci were found in the blood. In rabbits and dogs a subcutaneous injection of 1 cubic centimetre of liquid-gelatin culture of the aureus usually produced an abscess at the point of inoculation. If the dose was increased to 5 cubic centimetres of the same culture the animals died in from eighteen to twenty hours. At the same time a local inflammation was found at the site of inoculation. In all of the fatal cases the pus-microbe was found in the blood. Of the culture of the streptococcus pyogenes it was found necessary to inject a considerable quantity in order to produce suppuration. Liquefied-gelatin cultures of the staphylococcus pyogenes aureus and albus, in doses of 1 cubic centimetre, injected into the abdominal cavity of rabbits, were well tolerated, and death was produced only when the dose was increased to from 4 to 6 cubic centimetres. Injection of cultures of the streptococcus pyogenes into the peritoneal cavity was even better tolerated, and usually had to be repeated several times before the animal died of septic peritonitis. A needle dipped into a culture of pus-microbes he could insert into points without causing suppuration; but the injection of from 0.3 to 0.5 cubic centimetre of a mixture of pus-microbes, suspended in distilled water, into the hip-joint of rabbits, was followed by suppurative arthritis, rupture of the capsule, and diffuse para-articular phlegmonous inflammation and suppuration, and often death of the animal. Injection of 1 or 2 drops of a liquefied-gelatin culture of the staphylococcus pyogenes aureus, or albus, into a vein of a rabbit did not produce any serious disturbance, but if the dose was increased to from 0.5 to 1 cubic centimetre, it, as a rule, caused fatal disease. In such cases, multiple suppurating foci were found in the kidneys, liver, spleen, and lungs, with pleuritis and peritoneal effusions, pericarditis, and myocarditis; also serous and purulent effusions into joints and muscular abscesses.

The effect of inoculation with pus-microbes in man is the same as in animals. Garré made a superficial abrasion on one of his fingers, and applied a pure culture of the staphylococcus pyogenes aureus; the only symptom observed was a slight redness eighteen to twenty-four hours after the inoculation. He then made three small incisions, and inoculated himself with a larger quantity of the culture, which was followed by superficial suppuration. Fehleissen repeated the same experiments upon himself with cultures of different kinds of pus-microbes, and, if he succeeded in causing suppuration, this was always slight. He also found minute doses, administered subcutaneously, harmless; while larger doses, suspended in water, almost without exception caused abscesses, and, in animals, very large doses produced death from sepsis before suppuration could take place. Brockhardt introduced a trace of a mixed culture of staphylococcus aureus and albus into the cutis of his left fore-finger; after forty-eight hours a small abscess had formed, which was opened, and in the pus the same microbes were demonstrated. Bumm injected a pure culture of the yellow staphylococcus into the subcutaneous tissue of his own arm, and into the arms of two other persons. In each instance an abscess developed, which varied from the size of a pigeon's egg to that of a man's fist, according to the time which elapsed before they were opened. In the pus of these abscesses the same pus-microbe which had been injected was found. The above observations are conclusive in showing that pus-microbes can be cultivated from the pus of every acute abscess, and that, in man and animals, the injection of a sufficient quantity of a pure culture into the tissues is followed by suppuration; and thus far positive proof has been furnished of the direct etiological relationship which exists between pus-microbes and suppuration. Rinne has recently published an account of his experiments, and his results are somewhat in conflict with the authorities quoted above. He frequently failed to produce suppurative inflammation, even when he injected a large quantity of a pure culture, and by repeating the injection from time to time. He is of the opinion that, when the absorptive capacity of the tissues is not diminished, the pus-microbes are removed too rapidly to produce their pathogenic effect. The effect of inoculation with pus-microbes will, of course, always vary, according to the quantity of the microbes and the local and general susceptibility of the animal experimented on. Watson Cheyne has shown most conclusively that the number of bacteria introduced greatly modifies not only the intensity of the symptoms, but also the character of the disease. His experiments were made with cultivations of Hauser's *proteus vulgaris*. He estimated that $\frac{1}{10}$ cubic centimetre of an undiluted culture of this microbe contains 225,000,000 bacteria, and when this quantity was injected into the muscular tissue of a rabbit it produced speedy death. A quantity of the same culture corresponding with $\frac{1}{40}$ cubic centimetre, administered in the same manner, caused an extensive abscess at the point of injection, and death of the animal in six or eight weeks. Doses of less than $\frac{1}{500}$ cubic centimetre produced no effect,—in fact, doses of less than $\frac{1}{12}$ to $\frac{1}{120}$ cubic centimetre, or, in other words, fewer than about 18,000,000 bacteria, seldom caused any positive result. The same author found that in the case of the staphylococcus pyogenes aureus it was necessary to inject something like 1,000,000,000 cocci into the muscles of rabbits, in order to cause a rapidly-fatal result, while 250,000,000 produced a small abscess. In the case of the tetanus bacillus, death did not occur in rabbits when fewer than 1000 bacilli were introduced. He believes, as does Rinne, that the action of the preformed ptomaines on the tissues modifies the result. It is, therefore, probable that, in the experiments in which injection of pus-microbes did not produce suppuration, an insufficient number of active microbes were used, and that where indifferent substances and chemical irritants caused suppuration the implanted or injected material was contaminated, or that infection at the point of injection occurred through the wound, or subsequently through the circulation. The latter method of injection should always be borne in mind in cases where the presence of an aseptic substance in the tissues has apparently been the cause of suppuration. The tissues altered by the action of chemical irritants constitute a foreign substance, which may determine localization of microbes floating in the circulation, while, at the same time, the chemical alterations which they have caused in the tissues have prepared a favorable soil for their reproduction. Of late a number of pathologists have gone one step farther, and maintain that pus-microbes are not the direct cause of suppuration, but that their presence is essential for the production of ptomaines, to which they attribute pyogenic properties. If certain pyogenic, aseptic, chemical substances can convert living cellular elements into pus-corpuscles, as has been asserted upon good authority, we should naturally expect that chemical substances produced by pus-microbes in inflamed tissue might possess the same pathogenic property, and we will briefly consider what is known in reference to

Ptomaines of Pus-Microbes as a Cause of Suppuration.—Grawitz and de Bary, after detailing the results of their experiments with injections of chemical irritants in their investigations on pus formation, give an account of their experiments with the ptomaines of pus-microbes. They maintain that these ptomaines, like chemical irritants, prepare the tissues for the growth and reproduction of pus-microbes. The action of these substances can be studied by injecting sterilized cultures of pus-microbes, in which the only active agents could be the preformed toxines. These observers injected 4 cubic centimetres of a sterilized culture of the staphylococcus pyogenes aureus under the skin of a dog, with the effect of causing suppuration. The pus was examined for microbes, but none were found. They assert that the presence of oxygen is of the greatest importance in the production of ptomaines. Grawitz experimented also with a pure preparation of cadaverin, prepared by Brieger from bacteria. Cadaverin is a colorless fluid, the chemical formula of which is identical with pentamethylendiomin; a 2½-per-cent. solution of this substance destroyed the staphylococcus pyogenes aureus in an hour, and a small quantity added to a culture of pus-microbes arrested further growth.

A solution absolutely free from microbes, injected under the skin of animals, according to strength and quantity used, produced cauterization or inflammation, terminating in suppuration or inflammatory œdema, followed by resolution and absorption. The pus produced by cadaverin contained no bacteria as long as the skin remained intact. The injection of a mixture of a solution of cadaverin and pus-microbes was always followed by a progressive phlegmonous inflammation. Scheuerlen was the first to study the local action of ptomaines on the tissues. He introduced into the subcutaneous connective tissue of rabbits aseptic glass capsules containing sterilized infusion of meat. The wounds healed by primary union. As soon as the capsules had become encysted, he broke off both ends of the capsule, so as to saturate the tissues in its immediate vicinity with the fluid it contained. Three to six weeks after implantation of the capsule an incision was made down to it, and the parts submitted to a thorough examination. The ends of the capsule were always found to contain a few drops of thin, yellow pus, which, under the microscope, showed all the characteristic appearances of that fluid. No inflammation of the surrounding tissues. Cultivation experiments with the pus yielded negative results. It is evident that suppuration in these instances was caused by the action of the preformed ptomaines on the leucocytes and embryonal cells, and that its extension did not occur because the cause did not multiply in the tissues. In about twenty experiments the pus was found only inside of the capsule. Weigert has repeatedly shown that the difference between a purulent and fibrinous exudation can be readily demonstrated, as the former does not coagulate, although white corpuscles and plasma may be present.

Klemperer believes that this difference is due to previous destruction of fibrogen in the pus by the pus-microbes. The putrid-meat infusion used by Scheuerlen caused limited suppuration, and on that account it must also have possessed the property to prevent coagulation. To prove this he made the following experiment: The abdomen of a rabbit was opened while the animal was under the influence of chloroform, and blood was drawn directly from the aorta into a glass tube containing putrid extract of meat. As the fluids gradually became mixed the blood assumed a brownish-red color; coagulation did not occur for hours and days, while in the control experiments, with solution of salt, the blood coagulated firmly after the lapse of a few minutes. He next made thirty cultures of the staphylococcus pyogenes aureus upon agar-agar gelatin, and the same number of cultures of the albus, and after completion of their growth, fourteen days later, he sterilized them with boiling water, and, after shaking the fluid, removed the cultures and boiled them for a few minutes, and finally filtered them; he thus obtained about 150 cubic centimetres of a light-yellow fluid. This was reduced to 8 cubic centimetres by boiling; before using, the fluid was again filtered. The filtrate was put in capsules, and after sealing their ends hermetically they were inserted into the subcutaneous connective tissue of animals with the same care as in the preceding experiments. The suppuration which followed the breaking of the glass capsule in these cases was again found to be limited to the space with the capsule, being caused by action of the preformed ptomaines on leucocytes and embryonal cells, which found their way into the interior of the glass capsule.

The cadaverin and putrescin, two ptomaines prepared by Brieger, were next experimented with in the same manner. In preventing coagulation the results were even more striking than with the former substances. These experiments leave no doubt that ptomaines derived from pyogenic bacteria produce a chemical action on leucocytes and embryonal cells by which they are converted into pus-corpuscles. The suppuration thus produced, however, never extends beyond the tissues which are brought in contact with them, and, therefore, always remains circumscribed. *In this respect the results of the experiments just cited do not correspond with suppuration as we observe it in practice, as here from the same causes, and apparently often under the same conditions, the process presents the greatest possible variations in reference to its intensity and extent. In one case the suppuration remains circumscribed, resulting in a furuncle; in others the regional infection is more extensive, and a diffuse, phlegmonous inflammation is the result; while in the third class the local infection leads to general systemic invasion, and the patient dies of sepsis or pyæmia.* The clinical form of suppuration is noted for the progressive character of the infection, which is due to the reproduction of pus-microbes in the tissues and the production of ptomaines proportionate in amount to the number of microbes present, and, perhaps, also modified to a certain extent by the character of the soil. Practically, the matter remains the same as before it was known that the ptomaines produced in the tissues by the pyogenic micro-organisms could cause suppuration, as pus-microbes must be introduced into the organism, where they must also find an appropriate soil for their reproduction, before ptomaines can be produced in sufficient quantity to account for the occurrence of the clinical forms of suppuration. To the practical surgeon it is immaterial to know whether the transformation of leucocytes and embryonal cells is brought about by the direct action of pus-microbes or by the ptomaines which they produce in the tissues.

Description and Specific Action of the Different Pus-Microbes.—The microbes which, when present in sufficient number in the tissues, excite suppurative inflammation are called pus-microbes. Their effect on the cellular elements of the inflammatory product is a specific one, converting them into pus-corpuscles. Only such microbes will be described here which have been cultivated from pus, and the specific action of which has been demonstrated experimentally.

1. Staphylococcus Pyogenes Aureus.—The yellow staphylococcus is the microbe most frequently present in acute abscesses. Under the microscope it cannot be distinguished from the staphylococcus pyogenes albus.

It is easily cultivated upon gelatin, agar-agar, coagulated blood-serum, and potato. The culture liquefies gelatin. It grows best at a temperature approaching that of the blood, but can be cultivated at 30° C. It peptonizes albumen and coagulates milk. The culture grows in the track of the needle and upon the surface of the nutrient medium. The gold-yellow color of the culture appears only if the colony is exposed to atmospheric air. Cultures upon gelatin or agar-agar retain their virulence for a year or more. This coccus is met with frequently in acute circumscribed abscesses, osteomyelitis, pyæmia, and ulcerative endocarditis.

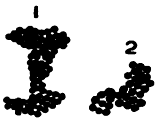

FIG. 49.—MICROSCOPIC PICTURES OF STAPHYLOCOCCUS. (*Rosenbach.*)

1, culture twenty-four hours; 2, culture two months.

2. Staphylococcus Pyogenes Albus.—This pus-microbe can be distinguished from the yellow coccus only by the color of the culture, which is white. Both Passet and Klebs have observed in the white culture of this coccus small yellow dots, which, when isolated, lost their color. These authors, therefore, consider the yellow and white staphylococcus as varieties of the same kind of pus-microbes. As other experimenters have not been able to verify these observations, we must take it for granted that the staphylococcus pyogenes albus differs from the aureus in that it possesses no power to produce the same yellow color which characterizes the culture of the latter. Its pathogenic properties, both in man and animals, are somewhat less than those of the aureus. Passet claims that the white coccus is more frequently found in the suppurative lesions in man than the yellow, while Rosenbach makes a contrary assertion. The latter author seldom found it alone in pus, but more frequently associated with the aureus. The cultures of both the yellow and white staphylococcus upon gelatin present an irregular surface, and the margins are dotted with minute globular projections. Both of these microbes liquefy gelatin, but agar-agar and coagulated blood-serum are not similarly affected.

3. Staphylococcus Pyogenes Citreus.—Found by Passet in about 10 per cent. of acute abscesses examined. Like the aureus and albus, it liquefies gelatin. Cocci singly, or in pairs, or zoöglœa. If cultivated on nutrient gelatin, or agar-agar, a sulphur or lemon-yellow growth develops after twenty-four hours, which at that time resembles the aureus, but later does not change into a gold-yellow color. Like the aureus, pigmentation only takes place if the culture is exposed to air. According to Passet, its virulence is somewhat less than that of the aureus and albus. This statement has been confirmed by Cheyne. When a culture of this pus-microbe is injected under the skin of mice, guinea-pigs, or rabbits, an abscess forms, from the pus of which a culture of the same lemon color can be obtained.

4. Staphylococcus Cereus Albus.—This microbe was first discovered by Passet in the pus of a periosteal abscess of a finger, as well as in an abscess of the heel. A culture upon gelatin is distinguished from that of other pus-microbes upon the same nutrient medium by its forming a white, slightly-shining layer, like drops of white wax, with a somewhat thickened, irregular edge. The needle-stab develops into a grayish-white, granular thread. In plate cultivations, on the first day, white points are observed, which spread themselves out on the surface to spots one-half a millimetre in diameter; when cultivated on blood-serum, a grayish-white, slightly-shining streak develops; and on potato the cocci form a layer which is similarly colored. This microbe is not pathogenic in rabbits.

5. Staphylococcus Cereus Flavus.—Passet cultivated this microbe from the pus of a case of chronic periostitis of the tibia. If cultivated on gelatin, the growth, which is at first white, becomes of a citron-yellow color, resembling somewhat yellow wax, considerably darker than the culture of staphylococcus pyogenes citreus. Both varieties of staphylococcus cereus are very rarely met with in abscesses, and inoculation experiments with them have usually proved harmless. Baumgarten thinks it possible that in cases where they were found in abscesses they were not the cause of suppuration, but occurred as an accidental invasion after the pyogenic microbes had disappeared.

6. Staphylococcus Flavescens.—This microbe was found in an abscess by Babes, and occupies an intermediate position between the staphylococcus pyogenes aureus and albus. On gelatin, the growth forms a colorless layer and causes liquefaction. It is fatal to mice, sometimes causing abscesses, and, in large doses, septicæmia.

7. Micrococcus Pyogenes Tenuis.—Rosenbach found this micro-organism in a large abscess which had given rise to no general symptoms. It is of rare occurrence. On agar-agar it forms an exceedingly delicate, almost invisible, white film. The individual cocci are irregular in shape, and larger than the staphylococci.

In all cases in which this microbe is the sole bacterial cause of suppuration, the process appears to have been unattended by any very severe inflammatory symptoms, and little or no general febrile disturbances. This microbe was not found by any one else but Rosenbach until February, 1888, when Raskina isolated it from the pus and organs in a case of scarlatina complicated with pyæmia, which resulted fatally on the eighteenth day after the beginning of the primary disease. At the necropsy multiple miliary abscesses were found in the kidneys, at the junction of the cortex with the medullary portion. From the pus of these abscesses a pure culture of the micrococcus was obtained. Inoculation experiments made on rabbits gave only negative results, even though the coccus was present in the blood twenty-four hours after inoculation; hence it is problematical as to its being a pyogenic microbe. Like the staphylococcus cereus, it probably belongs to the so-called *metabiotic* microbes of Garré, occurring secondarily after suppuration has been established by genuine pyogenic microbes.

8. Streptococcus Pyogenes.—Cocci, somewhat larger than staphylococci, always divide transversely, so that they arrange themselves in the form of chains, which are usually more or less curved.

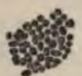

FIG. 50.—MICROCOCCUS PYOGENES TENUIS, CULTIVATED FROM PUS IN A CASE OF EMPYEMA. (*Rosenbach.*)

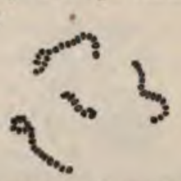

FIG. 51.—MICROSCOPIC PICTURE OF STREPTOCOCCUS PYOGENES. (*Rosenbach.*)

The cocci also appear singly or as diplococci. Cultures grow very slowly on ordinary nutrient media at summer temperature, but with great rapidity at the temperature of the body. Cultivated in a streak on the surface of gelatin on a glass plate, this microbe forms at first whitish, somewhat transparent, rounded spots, of the size of small grains of sand. On agar-agar it grows most luxuriantly at a temperature of 35° to 37° C. Even if the inoculation is made with the point of a needle in a continuous line, the culture appears in isolated, small points. In its further growth the culture is elevated in the centre, and presents a pale, brownish color, while the periphery is flattened, except at the extreme margin, which is again raised, and often with a spotted appearance. Still later, the periphery develops successive layers or terraces, which were pointed out by Rosenbach as characteristic macroscopical features of the cultures of this microbe upon solid nutrient media. The growth is so slow that in two or three weeks the maximum width of the culture streak is about 2 or 3 millimetres. In a vacuum the streptococcus effects peptonization of albumen and beef. Subcutaneous inoculation in mice yields negative results in about 80 per cent.; sometimes a slight suppuration follows at the seat of puncture, at times the animal dies without showing any particular pathological lesions, and no micro-organisms can be found in any of the internal organs. In the subcutaneous tissue of rabbits in small quantities they cause hyperæmia, redness, and slight swelling, which disappear in the course of two or three days; when larger quantities are used, some authors claim that they produce small circumscribed abscesses. In healthy rabbits intra-venous injection of even a pure culture of the streptococcus causes no serious symptoms. If the animals are debilitated previously by injections of toxic substances, death was caused by rapid reproduction of the microbe in the tissues. If a pure culture is injected into a serous cavity, it causes, first, inflammation, and, later, effusion, which is again absorbed. In the pus from the human subject the streptococcus is found in about 40 to 60 per cent. of the specimens examined. This pus-microbe invades the tissues far in advance of suppuration. It is found most frequently in inflammations following the lymphatic channels. It is also found in grave affections, in progressive gangrene. In several cases of pyæmia cultures of the pus yielded a growth composed exclusively of the streptococcus.

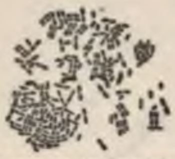

FIG. 52.—BACILLUS PYOGENES FŒTIDUS. ×790. (*Fluegge.*)

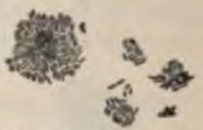

FIG. 53.—BACILLUS PYOCYANEUS. ×700. (*Fluegge.*)

9. Bacillus Pyogenes Fœtidus.—Passet found this micro-organism in the pus of a perirectal abscess. This bacillus possesses slow motion, its ends are rounded, and in cultures appears usually in pairs.

In stained specimens each bacillus shows in its interior one or two spores. This bacillus grows on gelatin, forming a delicate white or grayish layer on the surface, but causes no liquefaction. When cultivated on agar-agar and potato it has the appearance of a light-brown, glistening layer, which emits a very offensive odor. In mice traces of the culture do no harm; the injection of several drops causes septicæmia. Injection of about 10 minims of the culture into guinea-pigs causes an abscess, in which the bacilli alone are found as pyogenic cause; direct intra-venous injection causes sepsis.

10. Bacillus Pyocyaneus.—It has been known for a long time that the greenish-blue color of the pus, occasionally found in the pus of suppurating wounds, is due to the presence of a color-producing microbe.

The investigations of Gessard and Charrin, Ernst, Fordos, and Ledderhose have shown that this chromatogenous microbe is the bacillus pyocyaneus. In the pus and on solid culture media the bacilli appear in pairs, small groups, or, what is more common, large masses, or zoöglœa.

This bacillus grows upon gelatin, which liquefies and is stained a greenish blue. It also grows vigorously on agar-agar and potato, both of these substances being stained a greenish hue. In milk it causes caseation, with subsequent peptonization of the casein and simultaneous appearance of ammonia, while the coloring material appears on the surface in the form of greenish-yellow spots. Fordos and Gessard isolated the coloring material which this bacillus produces, and called it pyocyanin. It is soluble in chloroform, and from a pure solution crystallizes in long, blue needles.

Fluegge asserts that this bacillus is devoid of pyogenic properties, and appears only as a harmless settler upon wounds. Ledderhose, by cultivating this bacillus upon a large scale, obtained a considerable quantity of pyocyanin, and by chemical analysis determined its formula to be $C_{14}H_{14}, N_2C$. In doses of 1 gramme, as muriate of pyocyanin, injected into the circulation of different animals, he observed no toxic symptoms. When a pure culture of the bacilli was injected, he produced suppurative inflammation, and attributes this result not to the presence of pyocyanin, but to other as yet unknown phlogistic and pyogenic substances elaborated by the bacillus in the tissues.

IV. PUS.

Pus is the liquefied product of suppurative inflammation. It can be defined as a dead or dying tissue composed of cells with a fluid intercellular substance. Pus is an opaque, creamy, yellowish-white or greenish-white fluid, which, in a recent state, shows a slightly-acid reaction, and, later, becomes alkaline by the formation of ammonia. If it is of a yellowish color, creamy consistence, and odorless, it is the *pus bonum vel laudabile* of the old authors. If it is thin and intimately mixed with blood it is called sanious or ichorous pus. If it contain but few pus-corpuscles and resemble serum, we speak of serous pus. Pus undergoing putrefaction from the presence of saprophytic bacteria is rendered fetid, and is then termed fetid pus. Pus mixed with the products of tubercular inflammation is designated tuberculous pus, and if mixed with the secretion of an inflamed mucous membrane it is defined as muco-pus. If pus is allowed to stand undisturbed for a number of hours in a test-tube, it separates into two parts; the upper, the liquid portion, is the pus-serum, or *liquor puris*, while the lower represents the solid constituents of the pus, the pus-corpuscles.

Pus-serum.—The pus-serum contains albumen, a compound called pyine, regarded by Mulder as identical with tritoxide of protein, occasionally chondrin, glutin, and leucine, abundant fatty matter, and inorganic substances similar to those dissolved in the liquor sanguinis. Pus-serum contains no oxygen or hydrogen, or if present these gases are found only in minute quantities. On the other hand, it contains nitrogen and carbonic acid in large amounts. It contains more potash and soda than blood-serum. Among the albuminous substances which it contains are paraglobin, albuminate of potash, serum, albumen, and myosin. Pus-serum, in fact, is liquor sanguinis *plus* soluble compounds which have developed during the inflammatory process; hence it contains in solution the ptomaines elaborated by the pus-microbes.

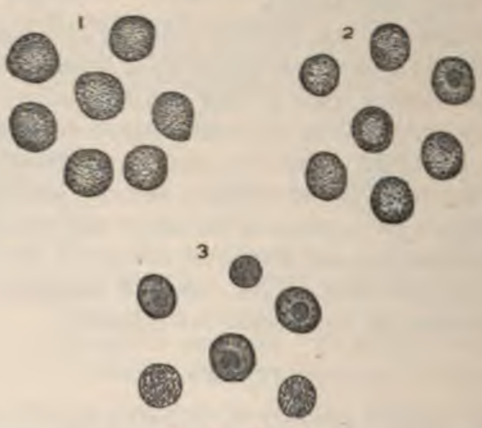

FIG. 54. (*Koch.*)

1, white corpuscles from normal blood; 2, pus-corpuscles with cocci in their interior; 3, pus-corpuscles with bacilli in their interior.

Pus-corpuscles.—The histological sources of pus-corpuscles are the leucocytes and embryonal cells. In acute inflammation the process is so rapid that the pus-corpuscles are derived almost exclusively from leucocytes. The conversion of a leucocyte into a pus-corpuscle in clinical suppuration is invariably accomplished by one or more kinds of pus-microbes which have been described. The pus-microbes constitute the most important morphological element of the product of suppurative inflammation, being not only diffused between the cells, but also find their way into the interior of the cells.

All pus-corpuscles show structural changes which indicate disintegration. The leucocytes present, as the first evidence of transformation into pus-corpuscles, fragmentation of the nucleus.

Nuclear fragmentation is an entirely different process from karyokinesis, as it is not, like the latter, an indication of cell reproduction, but of cell destruction. The nucleus breaks up into two to six or more fragments, the cell-body still retaining its original form. Fragmentation of the nucleus is attended by other forms of intra-cellular disintegration. The protoplasmic strings, which form a living reticulum in the interior of the nucleus and cell-body, break up and disintegrate. The embryonal cells, which are converted into pus-corpuscles, undergo similar retrograde changes, as have been described in the leucocyte. Pus-corpuscles are not always of the same size and shape. Their size will depend on their histological source. Those derived from leucocytes are somewhat uniform in size, while in subacute and chronic suppuration the fixed tissue-cells in a state of proliferation furnish a large percentage of the pus-corpuscles, and consequently their size varies according to the tissue-cells which undergo this change. As long as the leucocytes or embryonal tissue-cells are not completely destroyed by the pus-microbes or their ptomaines, they vary greatly in their shape.

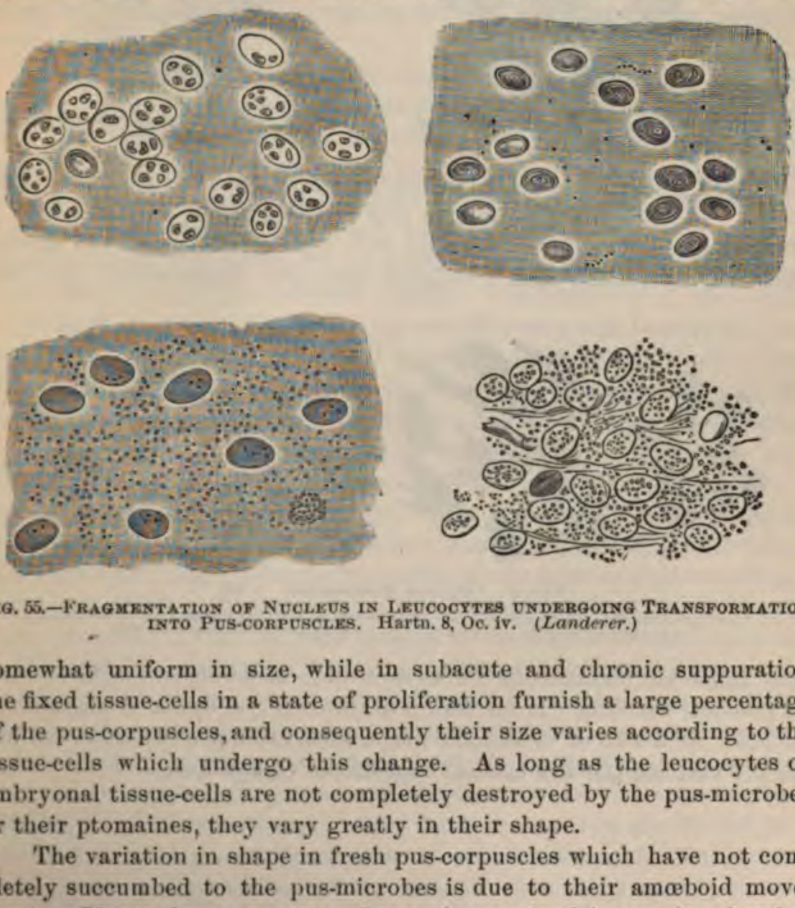

FIG. 55.—FRAGMENTATION OF NUCLEUS IN LEUCOCYTES UNDERGOING TRANSFORMATION INTO PUS-CORPUSCLES. Hartn. 8, Oc. iv. (*Landerer.*)

The variation in shape in fresh pus-corpuscles which have not completely succumbed to the pus-microbes is due to their amœboid movements. If pus from an acute abscess is examined in a moist chamber upon a warm slide, the amœboid movements of the pus-corpuscles can be observed for hours, provided the slide is kept at a proper temperature.

Pus-corpuscles subjected to the action of acetic acid clear up and show their fragmented nucleus much plainer. If pus-corpuscles are mixed with water they become larger and hydropic from imbibition of fluids. The round pus-corpuscles, according to Recklinghausen, are dead leucocytes or embryonal cells which have lost their amœboid movements. Liquor potassa dissolves the pus-corpuscles, and, if added to fluids containing pus, changes them into a gelatinous mass. In chronic abscesses the pus-corpuscles undergo molecular degeneration, and such pus under the microscope shows no well-formed corpuscles, but a mass of granular detritus. If the serum is absorbed, we speak of inspissation of pus. If a wall of cicatricial tissue form around a collection of pus, we say that the pus has become encysted or encapsulated.

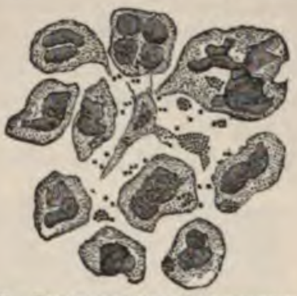

FIG. 56.—PUS WITH STAPHYLOCOCCUS. × 800. (*Fluegge.*)

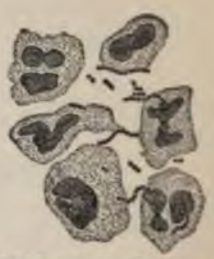

FIG. 57.—PUS WITH STREPTOCOCCUS. (*Fluegge.*)

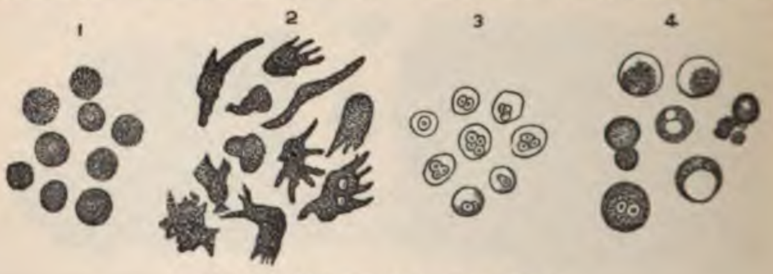

FIG. 58. (*Billroth-Winiwarter.*) × 400.

1, dead pus-corpuscles; 2, various forms which living pus-corpuscles assume by their amœboid movements; 3, pus-corpuscles acted upon by acetic acid; 4, pus-corpuscles after addition of water.

CHAPTER IX.

SUPPURATION (*continued*).

CLINICAL FORMS OF SUPPURATION.

IN reference to the time required to transform the product of inflammation into pus, suppuration can be divided into acute, subacute, and chronic.

I. Acute Suppuration.—In acute suppuration the wall of the capillary vessels is altered so seriously that emigration of the colorless corpuscles takes place with such rapidity that within a few hours the connective-tissue spaces are crowded with them, and in a few days the inflammatory swelling presents indications of approaching suppuration. The inflammatory swelling is hard to the touch, and the tissues around it become œdematous from obstruction to the plasma circulation within and in the immediate vicinity of the inflamed tissues. The hardness of the swelling is due to the infiltration of the connective tissue with leucocytès. In this form of suppuration a central ischæmic area is established by the rapid accumulation of leucocytes in the connective-tissue spaces, and, by pressure upon the inflamed and weakened capillary vessels, finally leads to complete stasis. The pus-microbes and preformed ptomaines are present in such large quantities that liquefaction of the inflammatory product takes place within a few days. The first appearances of suppuration are observed among the cellular elements which appeared first, which corresponds to a point in the centre of the inflammatory swelling, because at this point tissue nutrition has suffered most, and the inflammatory product has been exposed longest to the deleterious influences of the pus-microbes and their ptomaines. The direct causes of conversion of leucocytes into pus-corpuscles are the pus-microbes and their ptomaines, the pathogenic action of which on the tissues results in purulent liquefaction of the inflammatory product. Softening in the centre of an inflammatory swelling is almost an unerring sign of approaching suppuration. The central suppurating focus increases in size by the extension of the process of liquefaction in all directions, the leucocytes saturated with the ptomaines of the pus-microbes being rapidly transformed into pus-corpuscles. Acute suppuration is always accompanied by more or less necrosis of the fixed tissue-cells. The acute cell necrosis is the result of diminished blood-supply and the local toxic effect of the ptomaines of the pus-microbes. Necrosis occurring so constantly from the combined action of these two etiological factors in acute suppurative osteomyelitis furnishes a good illustration of this. In phlegmonous inflammation, from the smallest furuncle to the largest acute abscess, connective-tissue necrosis is a constant occurrence, following as an unavoidable sequence of acute suppuration. Acute suppuration is almost without exception attended by a complexus of symptoms, indicating the entrance of phlogistic substances from the inflamed tissues into the general circulation, such as fever, headache, thirst, loss of appetite, which usually subside with the removal of the primary cause. Acute osteomyelitis, acute suppurative inflammation of the large serous cavities and joints, and phlegmonous inflammation of different organs are excellent examples of what is understood by acute suppuration, from an etiological, pathological, and clinical stand-point.

2. Subacute Suppuration.—As acute inflammation may pass into a subacute form, so suppuration may be delayed in acute inflammation for days and weeks, if the indirect and direct causes which are concerned in the transformation of the cellular elements into pus-corpuscles are present, less in degree and intensity than in acute suppuration. The character and intensity of the primary microbic cause may determine a subacute type of inflammation from the beginning, and suppuration is correspondingly delayed. In subacute suppuration the tissues have more time to accommodate themselves to the presence of the inflammatory exudate, and hence tissue necrosis is a less constant occurrence, and, if present, it is less extensive. In subacute suppuration, at least, a part of the pus-corpuscles are derived from the fixed tissue-cells; while in acute suppuration central liquefaction of the inflammatory product often takes place within three or four days, the same stage in the subacute form is often not attained in as many weeks. As a rule, the general symptoms are also less severe.

3. Chronic Suppuration.—In acute and subacute suppuration the pus-corpuscles are derived, in the former almost exclusively, and in the latter largely, from the extravasated leucocytes. With few exceptions chronic suppuration occurs as the result of infection with pus-microbes of a pre-existing pathological product composed of granulation tissue. In such cases the embryonal tissue is the product of a specific inflammation caused by the presence of micro-organisms which possess no pyogenic properties, but which excite in the tissues a chronic inflammation, the product of which consists of granulation tissue. The bacillus of tuberculosis, the microbe of syphilis, and the actinomyces are good illustrations of this class of microbes. If a lesion caused by any of these microbes become the seat of infection with pus-microbes, the latter and their ptomaines are brought in contact with cells which are readily converted into pus-corpuscles. In chronic suppuration the pus-corpuscles are derived mostly from embryonal cells, and consequently they show a greater variety in size and shape than the pus-corpuscles found in an acute abscess. Purulent liquefaction of a mass of granulation tissue is the characteristic pathological feature of chronic suppuration. Embryonal cells derived from any of the fixed tissue-cells are converted into pus-corpuscles by the pus-microbes and their ptomaines in the same manner as the leucocytes in an acute abscess, only that this result is attained more slowly. In the majority of cases chronic suppuration is the result of infection with pus-microbes of a pre-existing granulating focus, the liquefied portion of which constitutes the contents of the chronic abscess. While an acute abscess is often developed in the course of a few days, and a subacute in as many weeks, it may require as many months or years for the products of a specific inflammation to be transformed into a chronic abscess.

Suppuration in Wounds.—Infection of a recent wound with a sufficient number of pus-microbes is followed by suppurative inflammation, which in its local and general manifestations resembles phlegmonous inflammation as it occurs without a wound. One of the earliest evidences that such infection has taken place is a profuse primary wound-secretion. This secretion is a mixture of blood and serum, and is secreted in excess on account of the inflamed capillaries being more permeable, and yielding more readily to the intra-vascular pressure. It is also possible that under these circumstances closure of the lumen of divided capillary vessels does not take place as promptly nor as completely as in aseptic wounds. Suppurative inflammation, when it attacks a recent wound, commences upon its surface, with which the microbes have been brought in contact, and the products of coagulation necrosis furnish a favorable soil for their growth and reproduction. In such a wound the process of granulation is either impeded or completely suspended until the acute symptoms have subsided, as the embryonal cells are converted into pus-corpuscles almost as soon as they are formed. From the surface of the wound the inflammation extends to the deeper tissues, the extension being usually along the connective tissue, fascia, and intermuscular septa. The parts in the immediate vicinity of the wound present the usual appearances of a phlegmonous inflammation. The pus which forms first contains dead leucocytes, while later the embryonal cells furnish an additional histological source for pus-corpuscles. Granulating wounds are usually considered exempt from infection with pus-microbes. While this may be true if the whole surface is covered with an uninterrupted, intact layer of healthy granulations, it is certainly not the case if the granulations are in any way injured or diseased. A slight injury, as probing, may create an infection-atrium, through which pus-microbes enter the deeper tissues, where they may become the cause of a suppurative inflammation. Under unfavorable vascular conditions the granulations are rendered hydropic, become flabby and anæmic,—conditions which impair their resistance to the action of pus-microbes,—which then convert the layer of embryonal cells most remote from the blood-supply into pus-corpuscles. The preformed ptomaines injure the subjacent cells, which in turn undergo the same fate, and thus an unhealthy, infected granulation surface becomes the cause of a secondary suppuration in wounds which indefinitely delays the healing process. If in a suppurating wound the pus-microbes attack a vein and produce a septic thrombo-phlebitis, the essential etiological condition for the occurrence of the most dangerous and intractable complication, pyæmia, has been established.

SUPPURATIVE INFLAMMATION OF MUCOUS MEMBRANES.

Suppurative inflammation of a mucous membrane is always preceded by a catarrhal stage, during which the amount of the physiological secretion is greatly increased. Proliferation of epithelial cells takes place with such great rapidity that the blood-supply becomes inadequate, when the most superficial embryonal cells readily succumb to the specific action of the pus-microbes and are exfoliated as pus-corpuscles. The ptomaines become diffused in advance of the microbic invasion, and, by injuring the protoplasm of the cells more deeply located, prepare the way for the pathogenic action of the pus-microbes, and suppuration extends more deeply. In this way ulcers form, which may remain superficial, or which may also penetrate deeply and result in perforation. The products of coagulation necrosis which form upon the surface of an inflamed mucous membrane favor the occurrence and extension of suppurative lesions, as they serve as a means of fixation and propagation of the pus-microbes. Pus from a suppurating mucous membrane, examined microscopically, will show pus-corpuscles derived from leucocytes and embryonal, epithelial, and connective-tissue cells which have become detached before they are converted into pus-cells.

1. Abscess.—An abscess is a collection of pus in the tissues. A collection of pus in a preformed space, such as the pleura, pericardium, Fallopian tubes, pelves of kidneys, etc., although resulting from a suppurative inflammation of the walls lining the space, is by general custom and usage not called an abscess, but the presence of pus in any of these organs is indicated by the prefix *pyo*, to which is added the anatomical locality—thus, pyo-thorax, pyo-pericardium, pyo-salpinx, pyo-nephrosis. The formation of an abscess is always preceded by a circumscribed suppurative inflammation. The histological conditions which are present at the time pus formation commences are characterized by a richness of leucocytes in the connective tissue between the inflamed capillary vessels and compression of the pre-existing tissue-cells by them and the transuded serum.

Suppuration commences at one or more points in the infiltrated area; if the latter is the case, the different suppurating foci soon become confluent, forming an abscess-cavity, which increases in size in all directions, both by the products of inflammation breaking down into pus and by the mechanical pressure of the exudation and transudation upon the surrounding tissues. The size of the abscess is determined by the nature of the primary cause of the inflammation, its location, and the degree of local and general resistance inherent in the tissues and the patient. The staphylococcus is found more frequently in circumscribed abscesses, while the streptococcus is more prone to give rise to diffuse purulent infiltration. A suppurating focus near a surface is not so likely to result in a large abscess as when it is more deeply located, as in the former case spontaneous evacuation in the direction offering the least resistance is an early occurrence, while in the latter instance such a termination is only possible after the abscess has reached considerable dimensions. An abscess which develops in tissues debilitated by a contusion or some antecedent lesions usually reaches greater dimensions than if it occur in otherwise healthy tissues. In patients whose strength

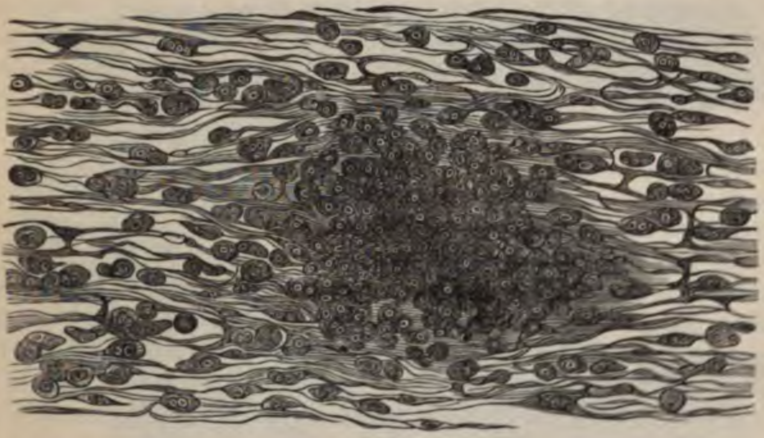

FIG. 59.—INFILTRATION OF CONNECTIVE TISSUE OF CUTIS, WITH BEGINNING SUPPURATION IN THE CENTRE. × 500. (*Billroth-Winiwarter.*)

has been impaired by old age, improper or insufficient food, intemperance, mental anxiety, or some antecedent acute or chronic ailment, it is well known that acute suppurative inflammation manifests a great tendency to rapid extension, while a vigorous, healthy body offers the most favorable conditions toward limitation of the suppurative inflammation. While liquefaction of the inflammatory product progresses from the centre toward its periphery, the outer zone of the inflamed area is in a condition of hyperæmia and active tissue proliferation. The leucocytes beyond the infected area are not converted into pus-corpuscles, and with the products of tissue proliferation constitute an impermeable wall, beyond which infection cannot extend. The limits of the abscess is an aseptic zone of infiltration, clinically readily recognized by its hardness to the sense of touch—the so-called abscess-wall. As many of the small vessels in the centre of the abscess are permanently destroyed, a collateral circulation is established in the abscess-wall and its immediate vicinity by the formation of new vessels, as is well shown in the above illustration.

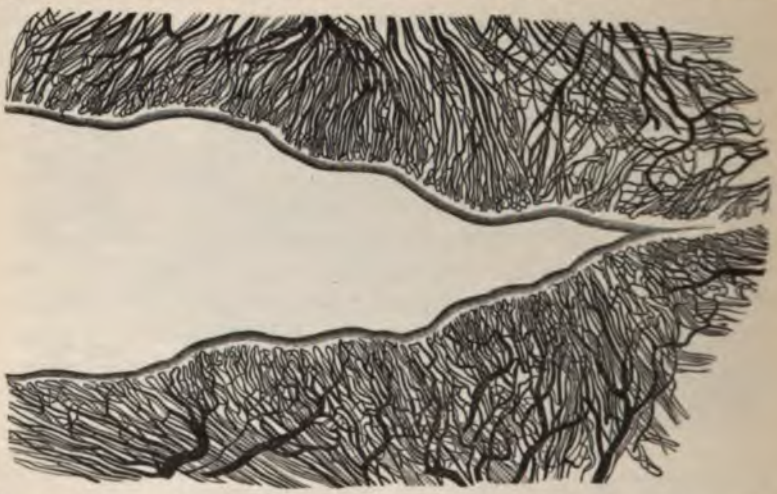

FIG. 60.—VESSELS (ARTIFICIALLY INJECTED) FROM WALLS OF AN ABSCESS ARTIFICIALLY PRODUCED IN THE TONGUE OF A DOG. × 25. (*Billroth-Winiwarter*).

According to their contents, causes, and the time which elapsed between the commencement of the disease which caused them and their formation, abscesses are divided into acute and chronic.

(a) Acute Abscess.—The acute or hot abscess is the usual termination of acute circumscribed suppurative inflammation. Its favorite location is in the connective tissue. It is always caused by infection with pus-microbes, most frequently the staphylococcus. It contains the characteristic yellowish, creamy pus, the *pus bonum et laudabile* of the old authors, and shreds of necrosed connective tissue. It appears within a few days after the commencement of the inflammation and reaches its maximum size in a short time. It is attended by the typical local and general symptoms which accompany acute suppurative inflammation. Acute abscess in the abdomen usually develops after perforation of the intestine or one of its appendages; thus, perforation of the gall-bladder often gives rise to circumscribed suppuration between the liver, stomach, and colon, and perforation of the appendix vermiformis in the right iliac region, where the circumscribed collection of pus is called a perityphlitic abscess. The loose connective tissue that surrounds the kidney is often the seat of an acute suppurative inflammation, giving rise to a perinephritic abscess. The connective tissue in front of the bladder, the so-called *cavum Retzii*, when it is infected with pus-microbes, occasionally becomes the starting-point of an acute abscess. In three cases of abscess in this locality, that came under my observation, the infection was caused by a perforation of an intestine, and in all of them, after incision, scraping, disinfection, and drainage, a fæcal fistula developed subsequently. Suppurative parametritis is another instance of acute abscess, and is usually caused by infection through the uterine cavity or the Fallopian tubes. Perirectal abscesses following suppurative paraproctitis are frequently preceded by localized rectal lesions, through which infection of the connective tissue surrounding the rectum with pus-microbes takes place. *The manner of invasion often determines the location and character of the abscess.* Thus, in suppurative mastitis, the abscesses which are caused by staphylococci always begin in the deeper part of the organ and extend toward the surface, while in infection with streptococci of the same part the inflammation shoots from some superficial abrasion and first attacks the skin, whence the process extends in a central direction to the deeper portions of the gland, where suppuration takes place (Cheyne). This difference depends on the manner of invasion of the two microbes. The staphylococci enter the organism through the milk-ducts and act from their interior, whereas the streptococci, like the microbe of erysipelas, enter the tissues through the lymphatic vessels, and their pathogenic action is primarily observed at the surface. Bumm excised a portion of the wall of a commencing abscess of the breast, and was able to demonstrate the presence of staphylococci in the interior of the acini, and their penetration thence into the inter-acinous tissue. The phlegmonous inflammation of the breast caused by streptococci takes place along the course of the lymphatics, and primarily involves the inter-acinous connective tissue.

Diagnosis.—The recognition of an acute abscess is usually not attended by any great difficulties. The history of an attack of acute suppurative inflammation is the first thing to be taken into consideration. Fever is usually present, but if the abscess has been caused by the micrococcus pyogenes tenuis it may be slight, or entirely absent. The location of the abscess has also considerable influence on the temperature. There is no doubt that the same kind and number of pus-microbes in some tissues produce either a larger quantity of phlogistic substances, or that these in some localities and certain tissues find a more ready entrance into the circulation. Pain is always present, but is variable in intensity according to the location of the abscess and the nature of its surroundings. It is severe if the abscess involves parts freely supplied with sensitive nerves, and where the inflammatory product gives rise to an unusual degree of tension. Thus, a small abscess underneath the deep fascia of a finger will cause more suffering than a large abscess in loose connective tissue. A beginning abscess can usually be accurately located by ascertaining the exact point of tenderness, on making pressure with the tip of a finger. If the abscess is sufficiently near the surface, fluctuation can be felt as soon as central liquefaction has occurred. Redness of the skin and diffuse œdema over and around the abscess are important symptoms, denoting the presence of pus. Remembering all the symptoms which point to the existence of abscess, in doubtful cases an absolute diagnosis should not be made by relying upon any one or all of them, as by doing so serious blunders have been and will be made in treatment. Aneurisms have been incised under the belief that they were abscesses, and the less serious mistake has been made of treating an abscess for an aneurism. The late Professor Gunn, who was well known as a careful and clever diagnostician, incised a large angioma in the occipital region, having mistaken it for an abscess. An inflammatory swelling occurring in localities where anuerisms are liable to be met with—that is, in the course of large blood-vessels—should be examined with the utmost care before an incision is made. The most difficult cases for diagnosis are the few instances where a suppurative inflammation occurs around an aneurismal sac. Fortunately, we are in possession of a very simple diagnostic expedient, which, if resorted to, as it should be, in all doubtful cases, will enable the surgeon, with infallible certainty, to ascertain the presence or absence of pus in an inflammatory swelling, and this is the use of the exploring syringe. An ordinary hypodermic needle with a long point will answer the purpose, although every surgeon should be supplied with an exploring syringe made for this special purpose. The needle must be rendered thoroughly aseptic by heating it in the flame of an alcohol-lamp. The surface where the puncture is to be made is thoroughly disinfected, and the needle is inserted somewhat obliquely toward the centre of the swelling and pushed boldly forward in this direction until resistance ceases, which is an indication that it has reached a cavity; the piston of the syringe is now slowly withdrawn and the fluid aspirated is examined; if it is pus the diagnosis is made and the needle is withdrawn. If no pus is found the exploration is carried deeper, and, if necessary, in different directions without removing the needle, by making aspiration at different points so as to explore the entire tracks made by the needle. If no positive diagnosis can be made it may become necessary to repeat this method of examination in a few days. A rapidly-growing sarcoma may simulate a suppurative inflammation so closely that great care is necessary to distinguish between these affections before any operative procedure is advised or undertaken. In exploring for pus in deep-seated abscesses in the abdomen or pelvis, care should be exercised to insert the needle in such a direction, whenever this is possible, as not to penetrate the free peritoneal cavity; whenever this cannot be done it should be introduced in such a manner that, after its removal, the puncture is sufficiently oblique to prevent the escape of pus. In such cases, it is always advisable to combine aspiration with exploration. If the tension in the abscess is diminished by removing a portion of its contents extravasation is less likely to occur.

Treatment.—A correct diagnosis made, the old rule *ubi pus ibi evacuo* is as applicable and wise to the treatment of an acute abscess at the present time as it was centuries ago. Nothing is gained by expectant treatment. The popular belief that an abscess should be drawn near the surface by the use of filthy poultices before it should be opened is fallacious both in theory and practice. An abscess is ready to be opened as soon as a sufficient quantity of pus has formed to constitute an abscess sufficient in size to be recognized by the surgeon as such. Students have generally been taught that an abscess should be evacuated by a free incision. This advice dates back to the time when antiseptics were not known and tubular drainage had never been heard of. The laying open of an acute abscess by an extensive incision is no longer necessary. The indications in the surgical treatment of an acute abscess are to open it in such a manner as to secure perfect evacuation and to resort to such means as will prevent re-accumulation of pus. These indications can be fulfilled much better by making multiple small incisions and establishing free drainage by the insertion of tubular drains, than by making a single long incision; at the same time, such treatment will leave the parts in better condition for rapid healing than by the old-fashioned incisions. The incisions need never be more than an inch in length, through which a rubber drainage-tube the size of the little finger can be readily introduced. Abscesses up to the size of an orange do not require more than one incision. Abscesses larger than this should be treated by through drainage wherever this is possible. In deep-seated abscesses the first incision is made at a point where fluctuation is most distinct, or in the direction of the track of the needle of the exploring syringe, if the pus has been located by the use of this instrument. Instead of incising the abscess with one stroke of the knife, I always incise the skin and fascia to the extent of an inch, and then with a pair of sharp-pointed and hæmostatic forceps I tunnel the intervening tissues. As soon as the point of the instrument has reached the abscess-cavity, pus will escape along the side of the instrument; the handles of the forceps are now locked and the blades separated sufficiently so that upon the withdrawal of the instrument the opening is enlarged sufficiently to introduce a drainage-tube of requisite diameter. If counter-openings are to be made, the same forceps is carried across the abscess-cavity and pushed from within outward at a point where drainage is most required, the skin over the point is cut with a knife, the opening dilated, and a drainage-tube drawn through. The surface over the abscess and a considerable distance beyond it should be shaved and disinfected before the abscess is opened. After incision and drainage the abscess-cavity is washed out with a weak antiseptic solution until the fluid returns clear, when an absorbent antiseptic dressing is applied. After twenty-four or forty-eight hours the dressing is removed, the drain shortened, or, if through drainage has been made, the drain is cut through in the middle and each opening is drained separately. If suppuration has not ceased the cavity is again irrigated. It is seldom that an abscess-cavity heals without further suppuration after it has been incised and drained, even under the strictest antiseptic precautions. The inner lining of the walls of the abscess remains infected with pus-microbes, and a limited suppuration, even in the most favorable cases, continues, at least until after the second dressing. The dressings should be so applied as to make equable compression, for the purpose of keeping the surfaces of the abscess-cavity in accurate apposition. The drainage-tubes are removed as soon as suppuration has ceased, when healing of the aseptic cavity takes place by granulation, in the manner described in the healing of wounds. An important element in the treatment of abscesses is to secure absolute rest for the part affected. Patients suffering from large abscesses should be kept in bed, and in the treatment of similar affections of one of the extremities rest is secured by the application of a well-padded splint, which will not only prove an efficient means of mitigating pain, but will keep the parts in a condition most conducive to rapid healing.

(b) Chronic Abscess.—Chronic, congestive, cold, or, as it is sometimes called, migrating abscess can most always be traced to some specific chronic inflammation, most frequently of a tubercular nature. What has been called a chronic abscess is very often no abscess at all. In tuberculous processes the product of tissue proliferation undergoes coagulation necrosis and disintegrates into a granular mass, which, when mixed with a sufficient quantity of serum, forms an emulsion that macroscopically resembles pus, but under the microscope shows none of the histological elements which are found in true pus. *An abscess can only be called such if it contain pus. A true chronic abscess can originate in a tubercular actinomycotic or syphilitic lesion when the granulation tissue is secondarily infected by the localization of pus-microbes, which convert the embryonal cells into pus-corpuscles.* Occasionally secondary infection with pus-microbes of such a granulating focus is followed by an acute phlegmonous inflammation, which extends rapidly to the surrounding tissues; but usually the suppurating process progresses slowly, and is not attended by any of the symptoms of acute inflammation. *What has been described as a cold abscess is a cavity containing the débris of the product of a tubercular inflammation, and is in communication with the primary lesion.* Such abscesses frequently appear at a distance from the primary seat of the disease. Thus, tuberculosis of the vertebræ gives rise to a lumbar abscess if the swelling appear in the lumbar region. It is called a psoas abscess if the tubercular product gravitate along the course of the psoas muscle and appear as an abscess underneath Poupart's ligament. Abscesses originating in the hip-joint often make their first appearance over the outer or inner aspect of the thigh, some distance below the joint. Abscesses originating in the shoulder-joint often wander a considerable distance away from the joint, along the course of the biceps or triceps muscle.

Bacteriological examination of the contents of such abscesses will show conclusively whether they are true pus-containing abscesses, or whether they are pseudo-abscesses. If cultivations are made with their contents, pus-microbes will grow upon proper nutrient media, if it is a true media, while from the contents of a pseudo-abscess only the microbes of the primary infection can be cultivated. The information obtained by the discovery of the essential cause can be confirmed by inoculation experiments. Cold abscesses, as a rule, are painless, not tender to the touch, and give rise to little or no febrile disturbances.

Diagnosis.—The diagnosis of a chronic abscess is based not so much upon the location, size, and characteristic features of the swelling as a careful consideration of the symptoms of the local lesion from which it started. Tubercular affections of the spine and hip-joints are accompanied by such well-defined symptoms at the stage when abscesses form that the primary lesion can be located without much difficulty. A chronic paranephric abscess often develops in the course of a tubercular pyelo-nephritis. A tubercular pelvic abscess is frequently associated with primary tuberculosis of the Fallopian tube. A chronic abscess often arises around a tubercular gland and appears, in consequence of infection with pus-microbes, as a chronic suppurative periadenitis. In such cases the gland itself has undergone caseation, and is often found extensively separated from the surrounding tissues by the suppurative process. In reference to the nature of the swelling and the character of its contents, an exploratory puncture will furnish positive diagnostic information.

Treatment.—The indications for early surgical interference in the treatment of chronic abscess are not so urgent as in the acute variety. These abscesses appear months and often years after the commencement of the primary disease. While an acute abscess should always be opened under antiseptic precautions, it becomes a matter of duty and conscience to deal with a chronic abscess in a surgical way, only under the strictest and most elaborate antiseptic precautions. It is a well-known clinical fact that when such an abscess opens spontaneously, or is incised in a careless way, profuse suppuration and hectic fever follow, with only too often a speedy fatal result from septic infection. Additional infection with pus-microbes results in the destruction of the granulations which line the cavity, and the patient dies from septic infection. Unless the surroundings of the patient admit of carrying out the antiseptic treatment to its fullest and most perfect extent, a chronic abscess should not be evacuated by incision. A number of German surgeons have recently advocated the treatment of such abscesses by aspiration and iodoform injections in preference to incision and drainage. One great difficulty in evacuating a tubercular abscess by aspiration is the blocking of the needle or trocar by shreds of necrosed tissue, which often interferes with complete evacuation. A chronic abscess should always be treated by incision, if by such procedure the primary lesion can be made accessible to direct treatment. If such a course is adopted, the incision is made large enough so that the whole cavity can be thoroughly scraped out and all of the infected tissues removed. After thoroughly curetting the cavity is cleansed and disinfected, and after drying it is iodoformized. The wound is then sutured, drained, and treated on the same principles as a recent wound. The treatment of special forms of chronic abscess will be considered more in detail in the chapter on Surgical Tuberculosis.

2. Phlegmonous Inflammation, with Suppuration.—Phlegmonous inflammation with suppuration is clinically characterized by rapid extension of the disease without leading to a circumscribed collection of pus or abscess. From the pus of this form of infection the streptococcus can be cultivated more frequently than the staphylococcus, and in some cases both of these microbes are found in the same pus. The inflammation affects the connective tissue, and extends rapidly along intermuscular septa, fascia, and tendon sheaths. This form of suppurative inflammation is prone to follow compound fractures, railroad and other crushing injuries, and all injuries attended by extensive contusion of connective tissue. The first symptoms usually appear within four days after the injury. The general symptoms are ushered in by a chill, followed by high temperature and rapid pulse. The first local symptoms are a copious, sanious discharge from the wound, and a rapidly-spreading œdema. The tissues are infiltrated with the same kind of fluid, and if life is prolonged sufficiently long a diffuse suppuration is inevitable. The symptoms of sepsis in this affection predominate because the pus-microbes have invaded an extensive area of tissue, and are reproduced with great rapidity and gain entrance into the general circulation at an early stage; at the same time the necrosed tissues, saturated with the bloody serum, furnish a good soil for the growth of putrefactive bacteria. In most of these cases the septic cellulitis is accompanied by lymphangitis, the parts presenting an erysipelatous appearance.

Treatment.—Phlegmonous inflammation of the type just described calls for early and energetic treatment before suppuration has appeared. The pus-microbes are present in such quantities that the connective tissue partially devitalized by an injury becomes necrosed from the local toxic action of the ptomaines of the pus-microbes. To render such wounds aseptic is one of the most difficult tasks in surgery. Small incisions and drainage will not accomplish the desired object. The infected tissues must be freely exposed by as many incisions as may be required. The secondary disinfection in such a case must be regarded in the light of a capital operation. The patient should be placed under the influence of an anæsthetic, the limb shaved and disinfected, and by large incisions the infected tissues must be rendered accessible to direct means of disinfection. Before undertaking the operation the limb should be rendered bloodless by applying Esmarch's constrictor.

In compound fractures the tissues immediately over the fragments should be incised sufficiently so that the fractured ends can be turned out. The infected medullary tissue should be scooped out with a sharp spoon, and all clots and necrosed tissue removed; the parts are then thoroughly irrigated with corrosive sublimate (1 to 1000), or car acid (1 to 20), after which the whole surface is dried and brush with a 10-per-cent. solution of chloride of zinc. Pockets and sinuses which cannot be reached with the sharp spoon can be rendered aseptic by pouring in peroxide of hydrogen, which, in such cases, is a remedy of great value. The bones are then placed in proper position, a number of counter-openings made, and a sufficient number of tubular drains introduced; after which a copious antiseptic dressing is applied and the limb properly immobilized, great care being taken to prevent decubitus or gangrene from pressure by protecting the parts exposed to pressure with antiseptic cotton.

During the subsequent treatment such a limb should be slightly elevated and suspended. If after such treatment the temperature is not lowered within six hours and the remaining symptoms are not improved, it is evident that the secondary disinfection has not succeeded in obtaining an aseptic condition of the wound. If amputation does not appear to be indicated at this time, another effort should be made to secure asepticity by resorting to permanent irrigation. The antiseptic dressing is removed and not re-applied. The parts are covered with a compress wrung out of a ½-per-cent. solution of acetate of aluminum, and constant irrigation made with the same solution. The simplest arrangement for constant irrigation is a reservoir holding the warm solution suspended over the patient's bed, and connected with the principal drainage-tube by means of a rubber tubing and a glass tip. By siphon action the fluid is conducted from the vessel to every part of the wound. The amount of fluid flowing through the tube can be regulated by compressing the tube to the desired extent with a clothes-pin. The limb being suspended, the fluid is conducted away from it into a vessel by means of a sheet of rubber cloth, macintosh, or gutta-percha.

Constant irrigation with a harmless, non-toxic, yet efficient germicidal solution in these cases is of the greatest value, as the wound-secretion is constantly washed away, and, as no accumulation can take place, the danger of sepsis from products of putrefaction is greatly diminished; at the same time the tissues are kept constantly saturated with the solution, which at last will exert a potent inhibitory influence upon the action and multiplication of pus-microbes in the living tissues. Should a faithful attempt at obtaining an aseptic condition by this method of treatment prove inefficient after a fair trial, the question of sacrificing a limb, to save, if possible, a life, will present itself.

In the absence of recognizable secondary foci in distant organs, the surgeon will not be able to ascertain whether a fatal form of general infection exists in a special case, and it is therefore always justifiable in resorting to a mutilating operation as a last resort, provided the patient's strength warrants such a procedure. As in cases of progressive gangrene, so in cases of progressive phlegmonous inflammation, it is exceedingly difficult to decide upon the exact location where the amputation should be made, as a distinct line of demarcation between healthy and infected tissues is never present. The only rule to go by in the selection of the site of amputation is to secure healthy skin-flaps, and to make the circular section of the muscular tissue above the tissues presenting macroscopical evidences of infection. The condition of the deep connective tissue furnishes important information concerning this question. The infection is sure to extend as far as any undermining or sloughing of connective tissue has taken place; hence, amputation should be done above these limits. The general treatment of phlegmonous inflammation is considered upon the same principles as the treatment of sepsis from other causes.

3. Progressive Purulent Infiltration.—This is the purulent œdema of Pirogoff. It is a more advanced stage of what has just been described as progressive phlegmonous inflammation with suppuration. Purulent infiltration follows upon the heels of phlegmonous inflammation, and is, consequently, clinically also noted for its progressive character. The infiltration is often very extensive, involving, in many cases, an entire extremity. It is always attended by extensive connective-tissue necrosis. The pus burrows deeply among the muscles and detaches the skin over a large surface. The external appearances seldom indicate the extent of the disease. If the skin is incised freely the parts beneath, the muscles, vessels, and nerves, appear as plainly as in a dissection made to show the relations of these parts. Purulent infiltration following progressive phlegmonous inflammation has often been mistaken for erysipelas, and has been called phlegmonous erysipelas. *If purulent infiltration complicate erysipelas, it occurs in consequence of secondary infection with pus-microbes, and not as a result of the action of the streptococcus of erysipelas.* The gravity of this disease depends largely upon the extent of the tissues involved. If it affect an entire limb the danger to life is great. Death may occur from pyæmia or exhaustion.

Treatment.—The surgical treatment is the same as in abscess, only that the incisions should be made longer, two or three inches in length, in order to enable the operator to remove the necrosed connective tissue and to insert large tubular drains. After the first incision is made a long, curved, Pean forceps is introduced, the cavity explored, and counter-openings made upon the point of the instrument in places where drainage will be most effective. The cavity must be drained at different points from one end to the other If the forceps is not long enough to reach both extremities it is removed and inserted again into the second opening, and so on until the cavity is thoroughly drained. It is advisable to bring each drainage-tube out of two openings and secure each end with a safety-pin. In cases of purulent infiltration of an entire lower extremity, I have often made as many as twelve incisions and inserted half as many drainage-tubes. After the cavity has been thoroughly drained, it is washed out with one of the milder antiseptic solutions. An excellent solution for this purpose is iodinized water. This can be readily prepared by adding tincture of iodine to sterilized water until the solution has the color of sherry wine. A solution of this strength is a valuable antiseptic, and can be used repeatedly and in large quantities without fear of causing intoxication. I have never succeeded in rendering such a large suppurative cavity aseptic with one irrigation, and have consequently abandoned the occlusive antiseptic dressings in these cases. It is much better to apply a compress wrung out of warm salicylated water or a 1-per-cent. solution of acetate of aluminum, which can be removed and re-applied every time the cavity is irrigated, which at first should be done every four to six hours. The warmth and moisture of the compress can be maintained by covering it with gutta-percha tissue or macintosh cloth. As burrowing of pus often does not stop even after efficient drainage has been established, the case should be watched with great care, and any attempt at burrowing should be promptly met by free incision and additional provision for drainage. It is always advisable to support the limb in proper position upon some kind of a suspension splint, both for the purpose of securing rest and to prevent contractures. As soon as suppuration has nearly ceased the drains are shortened and irrigations made less frequently. It is a consolation to know that such patients, especially if they are not advanced in years, and free from any other disease, often rally and make an excellent recovery after their strength has been reduced to a dangerous extent and their bodies reduced to a skeleton by the prolonged suppuration and septic fever. If suppuration is not controlled by drainage and antiseptic irrigation, and especially if the temperature and pulse indicate a continuance of absorption of septic material, amputation may become an unavoidable necessity. If amputation is decided upon, the deep incision must be made beyond the limits of the suppurating area. If the suppuration has extended as far as the hip-joint it may become necessary to utilize for flaps the skin which has been undermined, in order to secure a covering for the stump. If such a procedure become necessary, the internal surface of the skin-flaps must be rendered aseptic by using the sharp spoon and scissors in freeing it from infected tissue. During the whole course of the disease, which gives rise to purulent infiltration, the patient's strength must be supported by stimulants and tonics and a concentrated nutritious diet.

4. Suppurative Tendo-Vaginitis.—Another form of rapidly-spreading inflammation is suppurative tendo-vaginitis. As the name implies, it is an acute inflammation of tendon sheaths terminating in suppuration. It occurs most frequently in the tendon sheaths of the fingers, hand, and forearm. It develops usually from an infected wound of the finger or hand, or as a complication in the different forms of paronychia. The inflammation travels along the course of the tendon, starting, perhaps, from one of the tendons of a finger, extends to the palm of the hand underneath the annular ligament to the flexor muscles of the forearm, where it often produces a phlegmonous inflammation which, in the course of time, may involve the whole forearm. The tendons are often destroyed, and can be pulled out after a few weeks,—an occurrence which is always followed by permanent functional impairment of the affected finger or of the whole hand. Not infrequently suppurative inflammation of a tendon sheath extends to one or more joints over which the tendon passes, causing a complication, which often necessitates amputation. This affection is always attended by severe pain, and, if extensive, by grave constitutional disturbances. The extent of the disease can be ascertained, approximately, at least, by the external swelling, and especially by the tenderness along the course of the tendon. Frequently the inflammation attacks adjacent tendon sheaths and the pus undermines the entire palmar fascia.

Treatment.—The surgical treatment of suppurative tendo-vaginitis must be thorough if it shall be efficient. If it follow in the course of a wound, the tendon in the wound is exposed; if it develop during an attack of paronychia, it is laid bare by a free incision. Along the course of the tendon a curved forceps is passed, another incision is made down upon the point of the instrument, and a drainage-tube is drawn through. If the end of the suppurating cavity has not been reached the forceps is again introduced through the second incision down to the tendon, a third incision made higher up, and another drainage-tube drawn through. These manœuvres are repeated until the upper extremity of the suppurating cavity is reached. Taking it for granted that the suppurative tendo-vaginitis commenced in the distal portion of the middle finger, and has reached as far as the muscles of the forearm, the first drain should reach as far as the metacarpo-phalangeal joint, the second from here to the middle of the palm of the hand, the third from here to above the annular ligament, and the fourth as far as the middle of the forearm, and if suppuration has extended farther it will become necessary to extend drainage higher up by another drain. If the whole palmar fascia is undermined, a drain should be placed transversely across the hand. If the suppuration has extended to adjacent tendon sheaths, more extensive provision for drainage will be required. The subsequent treatment is the same as in cases of purulent infiltration. Necrosed tendons separate very slowly, but it is better to leave their elimination to the granulating process, as it is difficult to decide how much of the tendon should be removed, and its operative removal would often require large incisions, which would heal at best only slowly, and the large cicatrix would only add to the functional impairment of the member. From time to time traction can be made upon the tendon where it is exposed, so as to remove it as soon as it has become partially or completely detached. Passive motion and massage must be instituted as soon as the abscess has healed, so as to restore the function of the limb as far as compatible with the existing condition, as not only the affected finger but the whole hand often will be found to have suffered seriously from the attack. If one of the principal tendons of a finger has sloughed, and motion cannot be restored, it is advisable to immobilize the finger in a slightly-flexed position, as a curved finger is more serviceable than a straight one. Suppurative arthritis occurring in the course of an attack of tendo-vaginitis often necessitates amputation, more especially if it involve more than one joint of a finger.

5. Paronychia.—Paronychia, felon, whitlow, are terms used to designate an abscess of a finger. All of these terms should be abolished, and abscesses of the finger, like of other parts, should be called in accordance with the primary disease which caused them. Hueter made a classification upon a strictly pathological basis. The abscess may be located in the skin, and is then a furuncle; it may involve the connective tissue, and is then the product of a phlegmonous inflammation; it may form after an attack of periostitis or osteomyelitis, or, finally, it may commence in a joint, and is then from the beginning a suppurative arthritis. A suppurative tendo-vaginitis, as a primary affection of a tendon sheath, has often been mistaken for an ordinary felon, and treated as such, with most disastrous results. Suppurative tendo-vaginitis is frequently met with as a secondary affection of the different pathological conditions which give rise to abscess of the fingers. All of the conditions which have been enumerated as causes of abscess of the fingers are attended by excruciating pain, as the anatomical conditions necessary for the production of this symptom—tension and abundant supply of sensitive nerves—are pre-eminent in inflammatory affections of the fingers. The pain is of a throbbing character, and is always aggravated by placing the hand in a dependent position, as the venous congestion produced by this position increases the swelling, and consequently the tension, in the inflamed part.

Treatment.—Volumes have been written on the abortive treatment of paronychia,—the surest indication that none of the various means suggested have proved successful. Abscesses of the fingers, as in any other part of the body, result only from infection with pus-microbes; hence, any measure which falls short of effecting complete sterilization at the primary focus of infection must necessarily fail in accomplishing the desired object. The only rational treatment consists in the employment of such measures as will limit the extension of the suppuration. One of the most important elements in the early treatment of a felon is to diminish the blood-supply to the inflamed part by placing the limb in an elevated position, and by the continued application of cold. The use of ice in such a superficial inflammation will not only tend to diminish the congestion, but at the same time it has a positive influence in retarding the reproduction in the tissues of the primary cause—the pus-microbes. Poultices should never be employed. If position and the use of cold do not afford relief, moist, hot, antiseptic compresses should be applied. As soon as pus has formed it must be liberated by incision. The centre of the inflammatory focus is accurately located by marking out by pressure the area of tenderness, and the incision is made at this point parallel to the long axis of the finger. Scrupulous care must be exercised in rendering the whole surface of the finger aseptic before the incision is made. It is not good practice to make the incision invariably down to the bone, as the inflammation may not extend to this depth. The incision is only carried down to, but not beyond, the suppurating focus; hence, it is made down to the bone only if the abscess has originated in a joint, or has followed an osteomyelitis or periostitis of a phalanx. As the wound gaps, free drainage is not required. The abscess is washed out with an antiseptic solution, and the finger dressed antiseptically. Suppurative arthritis is treated by through drainage. In osteomyelitis followed by necrosis the sequestrum is allowed to separate and is then extracted, which can usually be done after three or four weeks. Excellent results are obtained after the loss of a complete phalanx, as the bone is often reproduced almost to perfection by the periosteal sheath. Amputation only becomes necessary in cases of osteomyelitis affecting more than one phalanx, complicated by suppurative arthritis of the adjacent parts.

6. Furuncle.—A furuncle is a small abscess of the skin. The centre of a furuncle is always occupied by a plug of necrosed connective tissue, vulgarly called a core. Longard has made a careful microscopico-bacteriological examination of 9 cases of furunculosis in young children. In 4 of these cases he found the staphylococcus pyogenes albus alone, in 5 cases in combination with the staphylococcus pyogenes aureus. The identity of these microbes with those described by Rosenbach was demonstrated by cultivation and experiments on rabbits. The microbes were not found in the fæcal discharges of the patients, but were discovered, in small numbers, in the diapers of healthy, unclean children, as well as in the diapers of those suffering from suppurative folliculitis. He believes that the pus-microbes are the direct and sole cause of the affection, and that infection takes place through the sweat-glands, as the microbes were found in abundance upon the inner surface of the *membrana propria* of these glands. As soon as the microbes reach the subcutaneous connective tissue they produce suppurative inflammation. Experiments on dogs and rabbits, by cutaneous inoculations with pus-microbes cultivated from the furuncles, produced a slight swelling and redness, and, in some instances, the formation of small pustules. The result of these inoculations was always the same, whether the cultures were made from the pus of a furuncle, a suppurating wound that healed without fever, or from a pyæmic patient. The inoculation experiments of Garrè, Brockhart, and Bumm, upon themselves, have been previously referred to, and they prove that many of the circumscribed suppurative affections of the skin (among them furuncle) are caused by the direct inoculation with pus-microbes, which enter the connective tissue either through a slight abrasion or through the glands of the skin. Furuncles often appear multiple, either in the same region or widely separated from each other over different parts of the body. In such cases the successive appearance of furuncles would tend to prove the reproduction and diffusion of the primary cause, the pus-microbes, over the surface of the body.

Treatment.—The prophylactic treatment consists in securing for the skin a healthy condition. By the free use of hot water and potash-soap the openings of the glands of the skin are cleared of accumulation of pus-microbes and of materials which might serve as culture substances. In patients suffering from furuncle, the slightest abrasions should be treated with care, in order to guard against infection. If the general health has been impaired, dietetic and medical treatment should be instituted to correct the faulty nutrition. We have no special internal remedies to correct a supposed suppurative diathesis which does not exist. Sulphide of calcium, which has been recommended in such strong terms, has no influence either in the prevention or cure of furuncles. With the first appearance of a furuncle, the skin over and considerably beyond it should be disinfected, and a compress saturated with a weak antiseptic solution applied. As soon as pus appears it is evacuated through a small incision, and if the necrosed tissue in its centre has become detached it is extracted. The interior of the small abscess is then disinfected and a small antiseptic dressing applied. A furuncle is an insignificant lesion, but its proper treatment should not be neglected, as numerous cases have been reported where thrombo-phlebitis, pyæmia, and acute suppurative osteomyelitis could be traced to infection from a furuncle.

7. Carbuncle.—A great deal of confusion has been created in the minds of students in reference to what is really meant by a carbuncle. This confusion has been brought about by the teachings of some of our text-books, both old and recent, which assert that carbuncle is always caused by infection with the bacillus of anthrax, while others speak of a less malignant form of carbuncle caused by suppurative inflammation. Malignant carbuncle, or malignant pustule, is the anthracic form of carbuncle, which always starts from a single centre of infection, and is always attended by necrosis of the overlying skin. The ordinary carbuncle, which is under consideration now, is caused by infection with pus-microbes, and differs from a furuncle only in so far that it is made up of a number of foci of suppuration, which develop simultaneously or in rapid succession, and usually become confluent. A carbuncle of this kind is in reality nothing else, etiologically and pathologically, but a group of furuncles. A section through a carbuncle, before extensive liquefaction has occurred, will show a number of foci of suppuration and necrosis, each one of which, taken separately, would represent a furuncle. On account of the more extensive area of infection in carbuncle than in furuncle, the local symptoms are much more severe. The tissues at an early stage become so extensively infiltrated that the carbuncle feels as hard as cartilage. The pain, as a rule, is very great. In size, a carbuncle varies greatly; it is sometimes not larger than a 25-cent piece, and it may attain a circumference fully as large as an ordinary soup-plate. The inflammation, which first attacks the skin and subcutaneous tissue, in unfavorable cases, extends to the deeper tissues and also travels in a peripheral direction. If the carbuncle is large, the skin covering it becomes gangrenous and extensive sloughing takes place. If the carbuncle is small, composed of only three to four centres of suppuration, the skin is not destroyed, with the exception, perhaps, of a very small portion, corresponding to the apex of each furuncular focus. Central necrosis of the connective tissue in each suppurating focus invariably occurs, and if the inflammation is very severe and extensive the whole carbuncle becomes a necrotic mass. In mild cases the tissues between the suppurating foci are preserved, and after the elimination of the necrosed tissue the part presents a cribriform appearance, each depression indicating the exact position of the former focus of infection. Carbuncle is met with more frequently in persons advanced in years, and attacks in preference such parts as are most exposed to infection from without, as the neck, face, and hands. The dangers to life connected with carbuncle are exhaustion and septicæmia, in the progressive form, while thrombo-phlebitis and pyæmia may occur as fatal complications even if the disease is circumscribed and the local symptoms not severe.

Diagnosis.—The differential diagnosis consists in separating carbuncle from furuncle and malignant pustule, or anthracic pustule. A furuncle presents only one centre of suppuration, is more circumscribed, more superficial, and not attended by such marked infiltration as carbuncle. Malignant pustule is primarily not a suppurating lesion, as it is caused by infection with the bacillus of anthrax, and develops from one point of infection and gives rise to necrosis of the skin at an early age. Carbuncle starts, simultaneously or in rapid succession, from three to a dozen or more suppurating foci, is attended by a hard induration of the surrounding connective tissue, and gives rise always to multiple foci of necrosis of the subcutaneous connective tissue.

Treatment.—The different methods advised at various times to abort a carbuncle have not proved more successful than the means suggested to check the growth of a furuncle. Very recently Beauquinque has made the assertion that a carbuncle can be aborted by applying to the part antiseptics dissolved in alcohol. He claims to have succeeded in three cases by applying tincture of iodine. While we have no right to question the correctness of his diagnosis, or the truth of his assertions, it is well known that the same treatment has not been attended by the same satisfactory results in the hands of other surgeons. It is difficult to conceive how the external application of tincture of iodine or any other antiseptic alcoholic solution should have the power to destroy the pus-microbes or prevent their reproduction when so deeply buried in the tissues. The most potent agent to limit the extension of the inflammation is the continued application of ice. As soon as pus has formed, the different foci of suppuration should be exposed to direct means of disinfection by incising the carbuncle under strict antiseptic precautions. The old-fashioned conical incision answers an excellent purpose. The necrosed and infected tissues are removed with a sharp spoon, and the surface is disinfected by irrigation with a solution of carbolic acid or sublimate; after which the scraped surface is dried and touched with a 10-per-cent. solution of chloride of zinc and the part covered with an antiseptic moist compress or dressed on strict antiseptic principles. If the primary disinfection does not arrest further extension of the disease, the whole surface should be deeply cauterized with the knife-point of Paquelin's cautery. After cauterization a compress saturated with a weak solution of corrosive sublimate is to be applied. With the cessation of suppuration granulations appear, when the same treatment is to be followed as in the management of granulating wounds. Septic thrombo-phlebitis is announced by a well-marked chill, followed by the usual grave symptoms which attend pyæmia. If the thrombosed vein can be located in such cases it should be removed by excision, with a faint hope that by an early recourse to this expedient a fatal form of pyæmia may possibly be prevented.

CHAPTER X.

SUPPURATIVE OSTEOMYELITIS.

SUPPURATIVE INFLAMMATION of the marrow of bone is an exceedingly frequent affection in children and young adults. As a primary disease it is seldom met with after the skeleton has become fully developed. The form of osteomyelitis that will be considered here is the so-called spontaneous variety, which occurs without direct exposure of the medulla to infective micro-organisms from without.

HISTORY.

Traumatic osteomyelitis following amputation, compound fractures, or gunshot injuries of the bones has been recognized for a long time as a distinct and serious wound complication, but osteomyelitis occurring without such injuries was not understood until quite recently. We find no mention of this acute affection of bone until 1705, when J. L. Petit gave a description of an acute disease of the long bones which corresponds with what we now understand by osteomyelitis. Similar allusions have been made to it by Gooch, Pott, Cheselden, Hey, and Abernethy, some of their descriptions being sufficiently accurate to enable us to recognize the character of the lesion. In 1831, M. Renaud published a paper "On Inflammation of the Medullary Tissue of the Long Bones," in which he gives a report of 5 cases occurring after amputation, all having terminated fatally.

Cruveilhier alludes to the remote consequence of this affection when he says, "The phlebitis of the bones is one of the most frequent causes of visceral abscesses following wounds or surgical operations in which the bones are involved." Roux credits Nélaton with having devised the term osteomyelitis in 1834, and having published a brief account of it in 1844. In 1849, Mr. Stanley, in his excellent monograph, "On Diseases of the Bones," gave an accurate account of the spontaneous variety under the title, "Suppuration in Bone." In 1855, Chassaignac applied the term osteomyelitis for the first time to the spontaneous variety, reporting at the same time 4 cases that came [illegible] observation. Among the surgeons who have increased our [illegible]umatic variety, the names of Vallette, M. [illegible], Lidell, and Allen deserve well-m [illegible] a complete *résumé*, in thirty propositions, of what was then known concerning the spontaneous variety. On account of the multiplicity of the bone affection, and the frequency with which the joints are involved, he called the disease "pseudo-rheumatism." The infectious origin of traumatic osteomyelitis has been recognized for a long time, but the spontaneous form was believed to be purely inflammatory until Luecke first called attention to its infectious character. Demme, Volkmann, Schede, and Hueter have added valuable contributions to the modern literature of non-traumatic acute suppurative osteomyelitis. Pasteur detected in osteomyelitic pus a microbe which he claimed was identical with the microbe found in furuncles; hence he spoke of osteomyelitis as "furuncle of bone." The bacteriological and experimental researches of Kocher, Rosenbach, Passet, Krause, and Kraske have established the fact that non-traumatic osteomyelitis, like the traumatic form, is a suppurative inflammation of the medullary tissue, caused invariably by infection with pus-microbes. *Primary suppuration in bone begins in the medullary tissue; hence it is not correct to speak of a suppurative ostitis, as is so frequently the case among English and American authors. Primary suppurative periostitis is an exceedingly rare affection; consequently, osteomyelitis must be considered as the most frequent of all inflammatory diseases of bone.*

BACTERIOLOGICAL AND EXPERIMENTAL INVESTIGATIONS.

Active suppurative inflammation in bone, when it occurs independently of an external wound, and consequently of direct infection, furnishes one of the most interesting, and, thanks to the patient and persevering investigations of a number of the foremost pathologists, one of the best-known forms of purulent infection. For years it has been contended, by some who made the etiology of acute osteomyelitis the subject of experimentation, that it is caused by a specific microbe not found in other forms of suppuration. Convincing evidence, however, has accumulated, which seems to leave no further doubt that the ordinary microbes of suppuration are the cause of this form of suppurative inflammation, and that the gravity of the symptoms which attended the disease, as compared with other suppurative processes, is owing to the anatomical location and structure of the inflamed tissues, rather than to any difference in the microbic cause. Even before the microbic cause of acute osteomyelitis was understood, Kocher believed that infection, in some cases at least, occurred through the intestinal canal, and made some experiments to prove this point. He produced subcutaneous fractures artificially in dogs, and then fed the animals large quantities of putrid material, and, in some cases, succeeded in causing suppuration at the seat of injury. In his clinical experience he also observed that in many cases of acute suppurative osteomyelitis the premonitory symptoms pointed to the gastro-intestinal canal as the *portio invasionis.*

Rosenbach cultivated the staphylococcus from osteomyelitic pus as early as 1881. In one case the yellow and the white staphylococcus were found together, in another case the staphylococcus alone, while in a third case the aureus and the streptococcus pyogenes were cultivated from the same pus. Rosenbach produced the same result in his experiments by injection of a pure culture of pus-microbes from a furuncle of the lip, as Struck did with cultivations from the pus of osteomyelitis, and with osteomyelitic pus injected into the subcutaneous connective tissue he produced an ordinary abscess. Recurrent attacks of osteomyelitis, years after the primary disease had been apparently cured, Rosenbach explains by assuming that after the first attack some of the microbes remain in the tissues in a latent condition until, at some subsequent time, local conditions are created which enable them again to display their pathogenic properties. Struck obtained from the pus of an acute case of osteomyelitis, upon gelatin, an orange-yellow culture; the identity of this culture with the staphylococcus pyogenes aureus was soon generally recognized. By injecting a pure culture into the circulation of animals which had been subjected, a few days before, to injury of bone, as contusion or fracture, he produced a suppurative inflammation at the seat of the trauma. Krause cultivated from osteomyelitic pus the staphylococcus pyogenes aureus and albus, which he also found in the effusion of joints, when this occurred as a complication of the disease. Injection of a pure culture of these cocci into the peritoneal cavity of animals caused suppurative peritonitis. Intra-venous injections, with or without previous fracture, were followed most frequently by suppuration in joints and muscles. If a bone was fractured subcutaneously before the injection was made, he frequently observed suppuration at the seat of fracture, and from the pus the staphylococcus could again be cultivated. Foci in the kidneys were always present in all of these experiments. Müller succeeded in cultivating the staphylococcus pyogenes aureus from the yellow granulations in cases of acute epiphyseary osteomyelitis. Rodet succeeded in producing in animals suppurative osteomyelitis by intra-venous injections of pus-microbes, without inflicting an osseous injury. The suppuration, which was generally circumscribed, was usually located near the epiphysis; it seldom involved any considerable portion of the shaft. In many cases separation of the epiphysis and suppurative arthritis of the adjacent joint occurred. In the most acute cases, the animal died within twenty-four hours, without any appreciable changes in the bones being demonstrable at the necropsy. Young animals proved more susceptible to inoculations.

Rodet believes that primary localization of the pus-microbes takes place in the medullary tissue at a point close to the epiphyseal cartilage. When separation of the epiphysis occurred, the pathological fracture was always found on the side of the diaphysis.

Rinne, who failed in producing metastatic abscesses with pure cultures of pus-microbes, rendered four rabbits pyæmic by injecting osteomyelitic pus directly into the venous circulation. He used the pus taken from a case of acute osteomyelitis with grave symptoms, and diluted it with distilled water, and of such a mixture he injected a Pravaz syringeful into one of the auricular veins of four rabbits. One died in twenty-four hours, with symptoms of toxæmia, and the autopsy showed nothing but a beginning pneumonia of left lung. The other three animals died seven to ten days after the injection, and in all of them suppurating foci were found in the kidneys and the muscles of the heart. No abscess in muscles or suppuration in joints. The plate cultures made from the pus used for the experiments showed the staphylococcus pyogenes aureus and albus and the bacillus pyocyaneus. With the exception of the albus, all of the microbes were also cultivated from the pus of the metastatic abscesses. In a later communication the same author expresses the opinion that the indirect causes of suppurative osteomyelitis are changes brought about in the medullary tissue by the microbes and their ptomaines of general febrile diseases, such as typhus, scarlatina, diphtheria, etc., which prepare the soil for the action of pus-microbes, or the disease is produced by the direct extension from a localized suppurative lesion, as a furuncle, through the lymphatic vessels, or along vessel- or nerve- sheaths to the medullary tissue.

Kraske has studied, from a clinical stand-point, the manner of infection in cases of acute osteomyelitis. In one case he could trace the infection distinctly to a furuncle of the lip; but, as a rule, he thinks that infection takes place through a wound or abrasion of the skin. Infection through the intestinal canal he considers possible, but not proven; more frequently it takes place through the respiratory organs, and in one case he could locate the infection through this route with certainty. He asserts that recurring attacks should not always be looked upon as the result of former infection, but as a consequence of a new infection of the old site.

CAUSES.

The essential exciting cause of suppurative osteomyelitis, both acute and chronic, is the presence of one or more varieties of pus-microbes. Direct extension of a suppurative lesion through the medium of lymphatic vessel- or nerve- sheaths, as Rinne suggests, may be possible, but such a direct connection between a peripheral suppurating focus and a central osseous lesion of a similar nature can seldom be demonstrated. *Infection in most instances takes place by pus-microbes, which have found their way into the circulation from a suppurating wound or through the respiratory or intestinal mucous membrane, and which localize in the medullary tissue prepared for their reception by anatomical peculiarities of the capillary vessels, or by a locus minoris resistentiæ, created by an injury or some antecedent pathological condition.* A number of well-authenticated cases have been reported where a subcutaneous fracture became the starting-point of an attack of osteomyelitis in patients who suffered at the same time from a suppurating wound in a part distant from the fracture. *In such cases it is reasonable and logical to assume that pus-microbes enter the circulation and are conveyed by the blood-current to the seat of fracture, where they are arrested and find a favorable soil for their reproduction and the exercise of their pathogenic properties.* Such cases are simply the counterpart of what has been accomplished by experimentation. *Clinical experience and experimental research have shown that pus-microbes localize in preference near the epiphyseal line of the long bones.* During the growth of bone this region is supplied with new, growing, and imperfectly-developed capillary vessels,—a condition which cannot fail in favoring localization of floating micro-organisms in this locality. Neumann has also called attention to a peculiarity of the capillary vessels in the medullary tissue, their calibre being four times greater than that of the arterial branches that supply them,—another important anatomical condition which predisposes to localization of microbes in this tissue. Histological investigation has also shown that the small blood-vessels in the medullary tissue are devoid of a proper vessel-wall, and appear more like channels or excavations than blood-vessels,—another condition which must yield a potent influence in determining congestion in these vessels and mural implantation of infected leucocytes under the action of an exciting cause or causes. As Luecke has shown, and as Rinne again asserts, the medullary tissue is prepared for the action of pus-microbes by the causes which precipitate an attack of some acute febrile affection, as variola, typhoid fever, scarlatina, rubeola, and diphtheria. Children and young adults who have passed through an attack of any one of these infectious diseases are strongly predisposed to an attack of acute suppurative osteomyelitis. Excluding all such influences, there is still left a large number of cases where osteomyelitis attacks persons otherwise apparently in perfect health. My own observations induce me to attribute to exposure to cold an important rôle as an exciting cause. I do not wish it to be understood that exposure to cold *alone could ever* result in an attack of acute suppuration of the medullary tissue. Pus-microbes inhabit persons in perfect health, and they do not cause disease as long as the circulation remains normal, as localization does not take place in the absence of a proper soil. If, however, in such a person the circulation in the medullary tissue is disturbed suddenly, in consequence of a sudden or prolonged chilling of the surface of the body-congestion, mural implantation and localization of the floating pus-microbes occur in a locality which offers the least resistance in such an emergency, and a suppurative inflammation is established in the medullary tissue. I have repeatedly observed cases of osteomyelitis in boys who, after active exercise, suddenly became chilled by bathing in cold water, or who, after an exciting game of base-ball, stretched themselves out on the cold ground to rest. A disturbance of the equilibrium of the circulation from any cause is an important factor not only in precipitating an attack of acute osteomyelitis, but many other local infective processes in persons already infected with the essential cause.

SYMPTOMS.

Acute suppurative osteomyelitis is usually ushered in by a chill and other symptoms indicative of the commencement of an acute suppurative affection. In some cases, even during the earliest stages, the general symptoms are out of all proportion to the local lesion, presenting a clinical picture characteristic of intense septic intoxication. I have observed several cases of multiple osteomyelitis, where the patients passed into a typhoid condition, muttering delirium, dry tongue, diarrhœa, and a continued form of fever, with a high temperature and rapid pulse, who died within a week, before the local disease had made any considerable progress. In one of these cases the patient was a young lady, 18 years of age, in whom the disease affected both tibiæ, 1 femur, both humeri, 1 clavicle, and several ribs from the very beginning, and the disease proved fatal on the sixth day. In such cases the prominent general symptoms are those of a malignant form of progressive sepsis. It is possible that the ptomaines produced by the pus-microbes in the medullary tissue may be more virulent, or that they are produced in larger quantities than in suppurative inflammation of other organs. Again, the ptomaines gain here more ready entrance into the circulation, as, at least in part, they are produced within the blood-vessels, and the extra-vascular products are forced rapidly into the circulation on account of the unyielding nature of the tissues around the primary focus of inflammation. In some cases of acute osteomyelitis the actual development of the disease is preceded by premonitory symptoms, which indicate the route through which infection has probably taken place. A preceding bronchial catarrh would indicate the possibility that infection had occurred through the mucous membrane of the respiratory organs, while infection through the intestinal canal would give rise to diarrhœa as a premonitory symptom. The local symptoms will be considered separately, as a correct early diagnosis can only be made by a careful study of these, individually and collectively.

Pain.—Pain is one of the earliest and constant symptoms of acute osteomyelitis. It may be absent in multiple osteomyelitis, where the patient passes into a condition of stupor almost from the beginning. The pain is described by the patient as being excruciating, of a boring, tearing, or throbbing character. It is not limited to the area involved by the disease, but is often diffuse, extending to the adjacent joint and over a considerable portion of the shaft. It is caused by the great tension resulting from the pressure of the inflammatory product in a tissue surrounded by an unyielding case of compact bone. Pain increases as the exudation becomes more abundant, and is diminished or subsides almost completely with the escape of the inflammatory product from the interior of the bone into the surrounding soft tissues. Sudden diminution of pain is almost a certain indication that perforation of the bone has occurred, and that the pus has escaped into the paraperiosteal tissues. The location of pain should be carefully inquired into, as in multiple osteomyelitis this symptom will locate, at an early time, the number and location of bones affected. In multiple osteomyelitis the disease may appear simultaneously in several bones far apart, or the disease appears in one bone first, and other bones are attacked later successively. The appearance of pain in a new locality is generally an indication that another bone has become involved.

Tenderness.—The patient is very seldom able to locate accurately the primary focus of the disease in an inflamed bone, as the pain is diffuse, but the pain caused by pressure will enable the surgeon to locate the primary focus within the bone with accuracy, even before any external swelling has appeared. *During the first few days the area of tenderness will correspond to the extent of the disease in the interior of the bone, and the centre of this area will correspond to the primary focus of the inflammation.* Tenderness is most acute where the disease has approached nearest the surface of the bone, and by this means the surgeon locates the site for early operation. Tenderness is caused by the secondary periostitis. In osteomyelitis of the long bones this symptom appears first near one of the epiphyses, and extends later toward the shaft of the bone as the periostitis ascends or descends in that direction.

Swelling.—The absence of external swelling during the first few days of an attack of acute osteomyelitis has often given rise to mistakes in diagnosis. As the primary inflammation is located in the interior of a bone, external swelling is absent until the inflammation has extended to the surrounding soft tissues. With the appearance of the secondary periostitis swelling occurs, which at first can be felt as a hard induration, soon followed by œdema and deep-seated fluctuation. The rapid local diffusion of the process is largely due to the unyielding nature of the tissues around the primary focus, and to the fact that the blood-vessels are directly concerned in the extension of the process by becoming the channels for the diffusion of the septic infection, their contents forming a nutrient medium for the pus-microbes. Thrombo-phlebitis is a constant and early condition in every case of acute osteomyelitis. The œdema of the soft parts is caused, in part at least, by the deep-seated venous obstruction. The external swelling seldom appears before the end of the first week, but when it once shows itself it increases very rapidly. The secondary suppurative periostitis results in extensive denudation of the bone of this membrane, a large portion of the shaft being surrounded by pus. As soon as the suppurative inflammation extends to the soft tissues, diffuse burrowing of pus takes place between the bone and the periosteum and among the muscles. Within a few days an immense abscess, or a very extensive purulent infiltration, develops in this manner.

Redness.—The skin over the affected bone presents a pale, normal appearance until the pus reaches the subcutaneous tissue, when it presents a red or brownish-red discoloration. The superficial veins are always dilated and turgid,—a reliable indication of the existence of a deep-seated thrombo-phlebitis.

Synovitis.—Inflammation of joints situated in close proximity to osteomyelitic foci is the rule. Catarrhal synovitis appears during the first few weeks, while suppurative synovitis usually occurs later as a complication of acute suppurative osteomyelitis. If the effusion into the joint is of a serous character, it occurs not as a result of infection with pus-microbes, but in consequence of vascular disturbances outside the limits of the area of infection. The serous effusion appears rapidly, gives rise to pain and contraction of the joint, but, as a rule, disappears spontaneously after the evacuation of pus. Suppurative synovitis follows infection of a joint with the same microbes that caused the osteomyelitis, which reach the joint either directly, through some pathological defect of the epiphysis, or through the lymphatics or blood-vessels. The occurrence of an attack of suppurative synovitis greatly aggravates the general symptoms, and is attended by more serious local disturbances than is the case if the effusion is of a non-septic character. If any doubt exist in reference to the character of the effusion an exploratory puncture will furnish the necessary information.

Epiphyseolysis.—Separation of an epiphysis from the diaphysis in the epiphyseal line is not an infrequent accident in cases of osteomyelitis of the long bones. It is a pathological fracture which occurs in consequence of necrosis, inflammatory osteoporosis, or molecular disintegration of bone in the epiphyseal line. It is readily recognized by the existence of a false point of motion and the displacements which usually attend fractures in such a locality. Epiphyseolysis seldom occurs before the end of the fourth or sixth week from the beginning of the attack.

Loss of Function.—In a limb the seat of an acute osteomyelitis all functions are usually completely suspended. It is as useless as though one of the principal bones had been fractured. The patient is unable to raise it, or to move the nearest joint. The limb is not only useless, but the patient complains of a sensation as though it would break on its being lifted or otherwise manipulated.

DIAGNOSIS.

Mr. Holmes has well said that acute suppurative osteomyelitis is more frequently recognized at post-mortem examinations than at the bedside of the sick. It has often been mistaken and treated for other affections, as periostitis, ostitis, inflammation of joints, rheumatism, typhoid fever, erysipelas, and even phlegmonous inflammation of the soft parts. When we remember that periostitis, ostitis, synovitis, and cellulitis are secondary lesions, intimately associated in the clinical history of every case of osteomyelitis, and, furthermore, that the fever attending it closely resembles typhoid fever, it is not surprising that mistakes in the early diagnosis of this disease are not infrequent, even in the practice of experienced surgeons. A careful consideration of every feature of the clinical picture presented by each case can only enable us to arrive at correct diagnostic conclusions. There is no single pathognomonic symptom that would infallibly lead us to a correct diagnosis. The presence of fat-globules in the pus was regarded as diagnostic by Chassaignac and Roser. Fat-globules are often found in osteomyelitic pus, but they are not invariably present, and may also occur in the pus of a phlegmonous inflammation. An important element in differential diagnosis is the absence of external swelling for the first few days, regardless of the severity of other symptoms; also, its rapid diffusion after it has once made its appearance. In periostitis and phlegmonous inflammation of the connective tissue, swelling is one of the earliest symptoms. In osteomyelitis the superficial swelling is at first œdematous, extends symmetrically around the entire bone, and gradually diminishes at a point where the morbid process in the interior of the bone has become arrested. In acute cases, fluctuation appears about the end of the first or during the second week. A consecutive inflammation of proximal joints usually makes its appearance about from the end of the first to the fourth week. The time of its appearance, as well as its character, is determined by the causes which produce the synovitis. While joint affections are almost constant in osteomyelitis, they are seldom associated with periostitis, or plastic osteomyelitis. The character of the fever which accompanies grave attacks of osteomyelitis sometimes obscures the local symptoms to such an extent as to lead the attendant to the belief that the patient is suffering from an attack of typhoid fever. Goltdammer has reported a typical case of this kind. The general symptoms simulated typhoid fever so closely that the patient, after an illness of ten days, was sent to the medical wards as a severe case of typhoid fever. The pulse ranged between 110 and 120; temperature, 40° to 41° C. Tympanites, dry tongue, enlargement of spleen, bronchitis, rapid respiration, and delirium. On close examination, a slight swelling was found over the lower part of the right tibia, with tenderness on pressure,—symptoms which finally enabled the attending physician to make a correct diagnosis. During the progress of the case, pleuritis, parotitis duplex, and synovitis of the right shoulder-joint made their appearance. The patient died eight days after admission, or eighteen days from the beginning of the disease. The necropsy revealed the existence of acute osteomyelitis of the tibia and pyæmia. Many such cases have been recorded where the differential diagnosis between acute osteomyelitis and typhoid fever was difficult, if not impossible, until the local symptoms became more prominent. The premonitory symptoms in typhoid fever are more constant and prominent than in osteomyelitis. In the latter affection the bronchial or intestinal catarrh which occasionally precedes the attack constitutes the only premonitory symptoms which have been observed, and, as a rule, the disease commences abruptly without any such warnings. Chassaignac believes that diarrhœa is present in almost all cases in the beginning, but it is a more constant symptom after septicæmia or pyæmia have made their appearance. The temperature, as a rule, shows less variation in osteomyelitis than in typhoid fever. After the initial chill and the usual symptoms attending the subsequent fever, the first symptom that points to osteomyelitis is pain. This is generally severe, deep-seated, constant, boring, tearing, or throbbing in character, and referred to the primary focus of the disease, usually in the vicinity of the epiphyseal line. Patients old enough to describe their sensations complain of a feeling as if the bone was being broken. They object to moving or handling of the limb on account of fear of an aggravation of this distressing sensation. E. von Wahl makes the statement that fluctuation is at first circumscribed in phlegmonous inflammation of the connective tissue, while it is diffuse from the beginning in osteomyelitis. This distinction is a good one. The importance of searching for points of tenderness in the diagnosis and location of the disease has already been alluded to. The differential diagnosis between rheumatism, gonorrhœal arthritis, and osteomyelitis is not difficult, as in the former diseases the joint affections occur as a primary disease, while in osteomyelitis they appear as complications.

PROGNOSIS.

Modern aggressive surgery has greatly diminished the mortality of acute osteomyelitis. Under the old, expectant, non-antiseptic treatment it was great. Thus, Demmé lost 4 out of 17 cases; Luecke, 11 out of 24; Kocher, 9 out of 26; and Schede, 3 out of 23 cases. Multiple osteomyelitis, with grave symptoms of septicæmia from the beginning, almost without exception proves fatal in less than two weeks. Death in such cases is caused by progressive sepsis resulting from the entrance of large quantities of pus-microbes into the circulation. After death no characteristic macroscopical lesions can be found in distant organs, and microscopical examination reveals only the minute changes in the capillary vessels typical of acute septicæmia. If the patient escape this, the first source of danger to life, he is still exposed during the duration of the acute symptoms to the more remote risks incident to the presence of septic thrombo-phlebitis. If any of the thrombi undergo softening and disintegration, fragments reach the general circulation and constitute infected emboli, which establish in distant organs, notably the lungs and kidneys, independent centres of suppuration,—the so-called metastatic or pyæmic abscesses. The accession of this fatal complication is announced by recurring chills, an intermittent form of fever, and is followed within a short time by death from sepsis or exhaustion. Another fatal accident which may occur is fat-embolism. The medullary tissue is liquefied by the suppurative inflammation, and some of the free fat-globules may be forced into the circulation by the intra-osseous pressure, and death is preceded by rapid, shallow breathing; cyanosis; small, rapid pulse,—symptoms which point to the existence of an obstruction to the passage of the blood from the right to the left side of the heart. Extensive destruction of the medullary tissue is always followed by marked anæmia, and this condition is a prominent symptom in all cases of osteomyelitis, as this disease seriously impairs the function of one of the important blood-producing organs. Schede has seen, in cases of acute osteomyelitis, the proportion of the white to the red blood-corpuscles increased to 1:100. The clinical thermometer is an important prognostic aid in this as well as in many other acute infective processes. If the morning and evening temperature remain continuously high,—that is to say, ranges between 40° to 40.5° C. during the first week,—it indicates a severe case. The more the general symptoms resemble a severe case of typhoid fever, the graver the prognosis. The occurrence of decubitus is always an unfavorable sign. In regard to the function of the limb after an attack of acute osteomyelitis, a few words are necessary. Necrosis of the bone to a greater or less extent is the rule. The extent of periosteal detachment during the acute stage is no indication of the area of subsequent sequestration, as the greater part of the denuded bone may receive an adequate blood-supply from the vessels within the bone, and soon becomes covered with granulations, and later unites with the periosteum or the paraperiosteal tissues. Joint affections and partial or complete separation of one or more epiphyses are frequent complications. A catarrhal effusion is generally removed by absorption, after the subsidence of the acute symptoms, and the functions of the joints are restored completely. If the effusion is sero-purulent and the articular cartilages remain intact, aspiration, with subsequent washing out of the joint with an antiseptic solution, may be sufficient to remove the effusion and restore the usefulness of the limb. Stiffness of the joint and malposition of the articular surfaces of the bones are events that cannot be avoided in all cases, even by the most skillful and attentive treatment. If the articular cartilages are destroyed by suppurative arthritis, the best result that can be hoped for is a useful but ankylosed joint. Pathological fractures through the shaft of a bone or epiphyseolysis are complications which greatly tax the duties of the attending surgeon, but from which the patients frequently recover with a useful limb.

PATHOLOGICAL ANATOMY.

Acute osteomyelitis is essentially a phlegmonous inflammation of the marrow of bone. This disease attacks, preferably, the long bones, although the scapula, clavicle, ribs, and ilium are also frequently affected, especially in cases of multiple osteomyelitis. Of the long bones the femur is most frequently affected. Seventy-three per cent. of all of Demmé's cases involved this bone. In the femur the disease manifests a special predilection for the lower epiphyseal region, while in the tibia the order of frequency is reversed. The great frequency with which the extremities of the shaft of the long bones are affected receives a plausible explanation from the activity of the physiological changes during the growth of bone, and perhaps to a lesser extent by the greater frequency of traumatism in these localities. Englisch claimed that the extremity of the shaft and epiphysis, toward which the nutrient artery is directed, is always primarily affected, on account of the greater blood-pressure in that locality. Clinical experience has proved the contrary. As acute osteomyelitis, without direct exposure of the marrow, is caused by infection with pus-microbes, which reach the tissue through the circulation, the inflammatory process must commence in the capillaries from mural implantation of microbes or leucocytes containing them.

The cause of the inflammation is primarily endo-vascular, and reaches the medullary tissue with the leucocytes. Intense alteration of the capillary wall is always present in these cases, giving rise to rhexis. Pus from acute osteomyelitis almost always presents a reddish appearance, which is owing to the presence of extravasated blood. The inflammation extends rapidly to the larger veins, which become blocked by the formation of a thrombus. If pus-microbes enter the thrombosed veins in sufficient quantity to cause liquefaction of the coagulated blood, pyæmia results from transportation of fragments of such infected thrombi to the distant circulation. Extensive thrombo-phlebitis results in arrest of circulation in portions of the bone, or perhaps of the entire shaft, which is followed by the usual consequences of such a condition—necrosis. Necrosis is undoubtedly also caused by the local toxic effect of the ptomaines of the pus-microbes upon the tissues and the pressure resulting from the presence of the inflammatory exudate in a tissue not capable of distention. The central medullary cavity is rapidly transformed into an abscess-cavity. The pus occupies either the entire cavity, a certain section of it, or in the form of multiple circumscribed abscesses or infiltration. The infection from the central focus extends along the blood-vessels and soon reaches the periosteum, which becomes the seat of an inflammation which resembles, pathologically, the medullary lesion in every respect primary. The secondary periostitis in every case of acute osteomyelitis always assumes a suppurative type. Pus accumulates between the periosteum and bone, causing often extensive denudation of the bone. The periosteum at some points is destroyed when the pus reaches the surrounding connective tissue, which then becomes the seat of a phlegmonous inflammation. The periosteal defects are not restored subsequently, and at these points openings remain later in the new bone, called cloacæ. After the active symptoms have subsided the suppurative periostitis gives way to a process of repair, during which the periosteum forms a case of new bone around the necrosed portion, which, in technical language is called an *involucrum*. The abscess in the soft parts heals, and one or more fistulous communications between the surface of the skin and the dead bone in the interior of the involucrum remain. The external openings are often quite distant from the cloacæ, and in such cases it is difficult, if not impossible, to discover the dead bone by probing. The necrosed bone is called a *sequestrum.* If necrosis has occurred at different points several sequestra will be included by the involucrum. Separation of a sequestrum, like the elimination of necrosed soft tissues, is accomplished either by suppuration or, what is more common, by granulation. Such pieces of bone always show an irregular or dentated outline, which is due either to the original shape of the sequestrum or to the action of the granulations, which diminish the size of the detached bone after its separation. Necrosis is said to be central if the sequestrum is composed of tissue from the interior of the bone, complete if it represent the entire thickness of the bone, and cortical if it is composed of the external compact layer only. In complete necrosis a pathological fracture necessarily takes place if separation occur before a firm involucrum has formed. In such cases restoration of the continuity of the bone is effected by the new bone. In central necrosis the dead bone is always encased in an involucrum. In cortical necrosis spontaneous elimination of the sequestrum frequently occurs if the bone separate before an involucrum forms around it, or, if an involucrum does not form, on account of destruction of a corresponding portion of the periosteum.

The medullary canal in the new bone, after central or total necrosis, is seldom restored to perfection. The new bone is harder and heavier than normal bone (osteosclerosis), but in exceptional cases it remains porous and soft (osteoporosis),—a condition described by Volkmann and Schede, which may become the cause of various degrees of deformity, from bending of the shaft. Separation of a sequestrum will take place in from four weeks to three months, according to the age of the patient and the location and extent of the necrosis.

TREATMENT.

An early and correct diagnosis is of the greatest importance in the treatment of acute osteomyelitis. As the gastro-intestinal canal is undoubtedly more frequently the route through which infection takes place than is generally supposed, and as nature's resources often attempt elimination of the pathogenic micro-organisms in this direction, it would appear rational to administer a brisk cathartic soon after the appearance of the first symptoms, as such treatment might prove of great value in arresting further infection from this source. A large dose of calomel, administered for the same purpose and in the same manner as advised during the early stage of typhoid fever, could not fail to produce a salutary effect. Kocher has advised the internal use of salicylate of soda, giving from 6 to 24 grammes in divided doses during twenty-four hours. In such doses this remedy would also have some effect in reducing the temperature, which is constantly high in all acute cases. Opium must be given in sufficient doses to alleviate pain. The affected limb should be placed in a slightly-elevated position.

Demmé, Billroth, and Volkmann recommend vesication by frequently-repeated applications of the strong tincture of iodine. It is doubtful if such treatment has any influence in arresting or even retarding the further development of the disease. The use of the ice-bag is rational, and often relieves pain. In multiple osteomyelitis, with pronounced symptoms of progressive sepsis almost from the beginning of the attack, it is doubtful whether any surgical treatment will have any effect in preventing a fatal termination. In such cases general infection occurs almost from the very beginning, and at the necropsy very little, if any, pus is found in the inflamed medullary tissue. The *indicatio vitalis* in these cases calls for the use of stimulants.

In regard to the propriety of making early incisions, the greatest diversity of opinion has prevailed in the past. Previous to the researches of Demmé, early and free incisions were practiced very generally. As the results following the treatment were frequently disastrous, Demmé was led to adopt a more conservative treatment. He advised an expectant plan to be pursued until the disease should exhaust itself, as it were, as indicated by reduction of temperature and cessation of the active symptoms of the inflammation, and then he argued the propriety of making large incisions. For the purpose of affording an outlet for the pus, Klose made early and small incisions at the junction of the epiphysis with the diaphysis. Ollier advocates early incision, combined with trephining of the bone. In a communication, read before the Academy of Paris, he claims that trephining is applicable to all forms of osteomyelitis with severe general symptoms. He maintains that trephining, even in the most diffuse form, will arrest the intense pain by relieving pressure; and where the disease is circumscribed it affords prompt and decided relief. In the acute form, he claims, trephining will often prevent external necrosis and fatal symptoms, while in the subacute and chronic forms it removes the most distressing symptom—pain. In 8 out of 19 cases of early trephining he found pus; and in 10 cases the marrow presented different, diverse, morbid appearances; while in the last case, a case of acute osteomyelitis of the femur, a large quantity of fluid blood escaped. Two of the 19 cases died of pyæmia.

Since osteomyelitis has been recognized as a microbic disease attempts have been made to arrest the disease by intra-osseous injections of germicidal solutions. Hueter has employed parenchymatous injections of solutions of carbolic acid with decided benefit in the treatment of other inflammatory affections of bones and soft tissues. Kocher recommended that the soft tissues around the infected bone should be disinfected by saturating them with a solution of carbolic acid, thrown in with an ordinary hypodermic syringe. Later, the same author suggested the propriety of making intra-osseous injections after penetrating the bone with a small perforation and injecting carbolized water, thus reaching the primary focus of the disease. Theoretically, the suggestion appears valuable; practically, intra-osseous injections in the treatment of acute suppurative osteomyelitis have proved a failure. If it is next to impossible to abort even a small circumscribed suppurative inflammation in the soft tissues with antiseptic parenchymatous injections, it is not surprising to learn that the same treatment has invariably failed in arresting suppuration in the interior of bones. Intra-osseous injections are no longer used in the treatment of acute suppurative osteomyelitis.

Antiseptic surgery has revolutionized the treatment of acute suppurative osteomyelitis. The diseased medulla is now attacked with the same impunity as the soft tissues outside of the bones. The objections to large incisions increasing the danger from sepsis and pyæmia are no longer well-founded, as incisions made under antiseptic precautions for the evacuation of pus, instead of increasing the risks of death from sepsis or pyæmia, are now considered the best means to prevent these fatal complications.

It can now be laid down as an axiom in surgery that the medullary cavity, in every case of acute suppurative osteomyelitis, should be freely exposed and submitted to direct and most thorough antiseptic treatment *as soon as a positive diagnosis can be made.* It would be a serious and unjustifiable mistake to open a healthy medullary cavity; but, on the other hand, it would also be next to criminal negligence to wait for fluctuation before resorting to operative treatment in a case of acute osteomyelitis. The bone should be opened, the infected medulla removed, and the cavity disinfected before suppuration has extended to the periosteum and the surrounding soft tissues. The intelligence and moral courage of a surgeon can be nowhere better tested and gauged than when he is confronted by a recent case of acute osteomyelitis. He must be sure of his diagnosis, and this often requires no ordinary erudition and diagnostic skill. A positive diagnosis made, he must possess enough courage to face the popular prejudice against early operation under circumstances where success is not always attainable. Impressed with the imperative necessity of operative interference from his knowledge of a case, a conscientious surgeon will not flinch from his duty, even under the most unpromising circumstances. If the responsibilities and risks are great, he will do well to fortify his course by calling into consultation one or more of his colleagues, to protect himself against unmerited criticism in the future, or, perchance, a suit for malpractice. An early radical operation for osteomyelitis (and the author means by this an operation done as soon as a positive diagnosis can be made, and before any external swelling has appeared) accomplishes the following most desirable results: 1. It removes pain. 2. It enables the surgeon to remove the local cause of the disease completely or in part. 3. It prevents extensive necrosis. 4. It is the best prophylactic measure against fatal septicæmia and pyæmia. 5. It prevents extensive destruction of the periosteum and other contiguous soft parts. 6. It cuts short the attack and expedites recovery.

As we have seen, the pain which attends osteomyelitis is caused by the intra-osseous tension and by the secondary periostitis. If the medullary cavity is opened freely before suppurative periostitis has developed, the operation removes the conditions which cause the pain, and will therefore accomplish at once what anodynes and external applications can do but imperfectly. The removal of the infected tissues fulfills the etiological indications of the disease, the removal of the pus-microbes completely or in part, which, with thorough disinfection of the cavity, prevents the further extension of the disease. Necrosis takes place from the action of the pus-microbes and their ptomaines on the tissues, intra-osseous tension, and vascular obstruction, all of which causes are either removed or, at least, favorably modified by an early radical operation. Limitation of necrosis is one of the most marked results of all early antiseptic operations for acute osteomyelitis. Progressive sepsis is caused by the introduction of pus-microbes and their ptomaines from the osteomyelitic focus into the general circulation; hence, there is no better way in which this fatal complication can be prevented than by the removal of the infected tissues and subsequent disinfection of the cavity, followed by efficient drainage and strict antiseptic treatment of the wound. As pyæmia is always caused by septic thrombo-phlebitis, no surer way of guarding against it could be devised than the early removal of the infected tissues, which may include the vessels with a beginning thrombo-phlebitis. If the interior of an osteomyelitic bone is rendered accessible to direct means of disinfection, such treatment will often, if not invariably, prevent the extension of the suppurative inflammation to the periosteum and surrounding connective tissue, which constantly occurs when the patients are treated upon the expectant plan. An early radical operation, by limiting the necrosis and extension of the inflammation to the surrounding soft tissues, shortens the attack, and is conducive toward establishing at an early time a reparative process in place of one of destruction. Pathological fractures will become less frequent complications in acute osteomyelitis as soon as early radical operations are more generally adopted. Early operations under antiseptic precautions, in short, are life-saving operations; at the same time, they will leave the parts in a more satisfactory condition for rapid and satisfactory repair. An early operation I should call one done before secondary suppurative periostitis has appeared. An intermediate operation for acute osteomyelitis is one performed after suppuration has occurred around the bone first affected, and late operations are undertaken for the removal of necrosed bone.

Early Operations.—The surface of the limb is prepared in the same manner as for other antiseptic operations. The primary focus of the disease, usually in the vicinity of an epiphyseal line, is accurately located by searching for the most tender point. Over this point, or as near to it as the nature of the soft parts will permit, an incision is made down to the bone. As the operation is to be done below Esmarch's constrictor, the soft tissues can be carefully examined during every step of the operation, and their exact condition ascertained. The skin and underlying fascia are cut through with one stroke of the knife, when the knife should be laid aside and the remaining tissues, down to the bone, are carefully separated with the finger, which can be readily done by following the intermuscular septa. The periosteum, even at an early stage, will be found vascular and easily separated from the bone. This structure is then reflected with the soft tissues on each side, and held out of the way with retractors. The bone is then opened with a small, round chisel. The trephine should never be used, as it is, to say the least, a bungling and inefficient instrument, while the chisel is an instrument of precision. For the first or exploratory opening a semicircular chisel should be used; in the further steps of the operation ordinary chisels, such as are used by carpenters, answer an excellent purpose. As the first opening will probably be made near an epiphyseal extremity, at a point where the compacta is very thin, the chiseling is attended by no difficulties. The opening is made directly toward the centre of the bone. If no pus has formed the osteomyelitic focus is recognized by the softness and great vascularity of the tissues and the escape of bloody serum. If pus is found it will probably appear at this time as an infiltration. The object of the operation is not only to open the bone, but to remove all of the infected tissues. The opening in the bone is, therefore, enlarged in the direction of the shaft to the extent of the disease in its interior. If the suppurative inflammation is extensive, involving half of the bone, or, perhaps, the entire shaft, it is advisable to make several incisions over the bone in the same line instead of one large incision, thus avoiding a large wound and, perhaps, injury of important structures; at the same time the interior of the bone is rendered accessible to direct treatment by opening the bone at the corresponding points and scraping out the medullary tissue contained in the intervening sections with a sharp spoon, the handle of which can be bent at any desirable angle. After the whole cavity has been thoroughly curetted it is disinfected by irrigating it with a solution of corrosive sublimate (1 to 1000), and then dried and mopped out with a 10-per-cent. solution of chloride of zinc. Peroxide of hydrogen is also an excellent remedy for disinfecting the bone-cavity after curetting. The cavity is then packed with iodoform gauze, which is brought out of the wound or wounds to serve the purposes of a capillary drain. A copious antiseptic dressing is applied, and the limb immobilized in proper position upon a splint. A fall in the temperature, and other signs of improvement soon after the operation, are indicative that the desired object, primary disinfection of the osteomyelitic focus, has been attained. If on the following day the temperature shows no reduction, the dressings are removed, antiseptic irrigations are again employed, and the limb is dressed antiseptically. Should, in spite of the early operation and careful antiseptic after-treatment, the suppurative inflammation extend to the periosteum and the connective tissue, the antiseptic occlusive dressing should give way to warm compresses kept saturated with one of the mild antiseptic solutions. Frequent irrigations with a 2-per-cent. boracic-acid solution, a $\frac{1}{2}$ to 1-per-cent. solution of acetate of aluminum, or a weak aqueous solution of tincture of iodine should be made, and the limb confined upon a suspension splint.

Intermediate Operations.—If a case of acute osteomyelitis come under treatment after purulent infiltration has occurred around the affected bone, no time should be lost in evacuating the pus by incision and drainage. Multiple incisions and numerous tubular drains are often required to effect complete evacuation and secure free drainage. In these cases operations on the bone itself should be limited to making smaller openings in the exposed portion of the bone, for the purpose of reaching its interior with antiseptic irrigations. Large openings, under these circumstances, might lead to pathological fractures. The subsequent treatment is conducted on the same principles as a case of phlegmonous inflammation and purulent inflammation of the soft parts.

As in the early treatment of osteomyelitis by radical operation, the limb must be supported in a desirable position by some kind of a splint. The use of a proper splint in the treatment of acute osteomyelitis is indispensable. A well-fitting posterior splint, or the anterior suspension splint of R. N. Smith, secures rest for the limb, prevents contractures and subluxation of joints, and finally diminishes the frequency of pathological fractures. Catarrhal synovitis is treated by aspiration, and suppurative synovitis by incision, drainage, and antiseptic irrigations. During the acute stage of suppurative osteomyelitis the removal of an entire shaft of a long bone should be limited to one bone of the forearm or leg, as the removal of the entire shaft of the humerus or femur before the formation of an involucrum of sufficient firmness to act as an efficient support would greatly complicate the mechanical part of the after-treatment, and the procedure might result in imperfect restoration of the bone removed. Where the greater portion or the entire shaft of a bone has become necrosed and has separated at one or both epiphyseal junctions, it may become necessary to remove it during the acute stage to avert death from exhaustion from profuse discharges and septic fever incident to the presence of such a large septic foreign body. It has been argued against such a procedure that the bone would not be regenerated after its removal. This fear, however, is not supported by facts, as when the periosteum and the epiphysis remain a good, if not perfect, substitute is reproduced. Duplay, Holmes, McDougal, Lefort, Giraldes, Spence, Pétrequin, Wilms, Cheever, Ropes, and Gay have each reported cases where almost complete reproduction followed the removal of the entire shaft. It is very important, especially in children, to preserve both epiphyses, to prevent subsequent shortening and other deformities of the limb. Where the continuity of a bone has been destroyed, either by a pathological fracture or the removal of a part or an entire diaphysis, which has separated before the involucrum has become sufficiently firm to serve the purpose of an efficient mechanical support, a suitable mechanical support must be applied for a long time to guard against shortening and bending of the new bone. During the septic stage of acute osteomyelitis with suppurative synovitis amputation may become necessary to save the life of the patient. In exceptional cases the same sad alternative may become a necessity after the acute symptoms have subsided, for the purpose of removing the source of exhausting suppurative discharges. Our present means of treating abscesses, diffuse purulent infiltrations, and suppurative diseases of joints are, fortunately, so perfect and efficient that even severe cases can be treated on a more conservative plan, and amputation should be restricted to extreme cases as a *dernier ressort*. Should signs of pyæmia arise, our main reliance must be placed on the administration of large doses of quinine and alcohol. Luecke has obtained the best results from large doses of alcoholic stimulants. Instances have been reported where two pint-bottles of cognac were given during twenty-four hours with decided benefit. Osteomyelitic patients should be surrounded by the most favorable hygienic influences, as fresh air, equable temperature, light, and an abundance of plain, nutritious food. As soon as the acute symptoms have subsided, iron, especially tinctura ferri chloridi, should be freely administered. If osteomyelitis is complicated by the co-existence of other diseases, such as syphilis, tuberculosis, rachitis, etc., the treatment of the latter should receive appropriate attention.

Late Operations.—As late operations will be considered the operative removal of sequestra. The operation for the removal of detached dead bone is called necrotomy or sequestrotomy. The operative removal of a sequestrum should always be postponed until complete separation has taken place and the involucrum is strong enough to furnish the necessary mechanical support. If an operation is undertaken at an earlier time there is danger of unnecessarily removing a portion of healthy bone or of leaving a part of the sequestrum. Necrosis is not a disease, but always a result of a destructive inflammation. It is not always easy to determine whether separation of the sequestrum has taken place in a given case. The sinus leading down to the dead bone may be so tortuous that it is impossible to introduce a probe into the interior of the involucrum. Again, if the sequestrum is felt with the probe it is often impossible, by any kind of manipulations, to ascertain in this manner its mobility, as it is often firmly encased in a bed of granulations. The time required in separation of the sequestrum varies greatly,—a whole phalanx of a finger may be separated completely in four weeks, a cortical sequestrum of a long bone may become detached in six weeks to two months, while the separation of half or an entire shaft of the large, long bones, as the femur or humerus, may require from three to six months. If the patient's general health is improving there is no need of haste in the removal of a sequestrum, as there is nothing lost and a great deal gained by waiting until sufficient time has elapsed for separation to take place. Sequestrotomy, if properly performed, is one of the most grateful of all operations, as it is attended by little or no danger to life, and is usually followed by a favorable result. Its performance has been greatly simplified by the use of anæsthetics and Esmarch's constrictor.

Since Esmarch taught us how to obtain, by a very simple appliance, a bloodless condition of the limb during the operation, the surgeon can make the necessary dissection with the same degree of accuracy as in the dissecting-room, thus avoiding injury of important vessels and nerves, which formerly occurred quite frequently even in the hands of the most accomplished surgeons. Before the operation the entire limb is disinfected and rendered bloodless by elevating it for a few minutes, when an Esmarch constrictor is applied on the proximal side and some distance from the seat of operation. I have met, in my practice, with 2 cases of paralysis of the musculo-spiral nerve from the use of Esmarch's constrictor, which was applied about the middle of the arm, and, although both patients recovered perfect use of the limb in the course of two to four months, I have since taken the precaution to guard against such a perplexing accident by applying the constrictor over the middle of the deltoids, and over several thicknesses of a towel in order to protect the nerves against undue pressure. Since I have made use of these precautions I have had no further accidents from elastic constriction. In an operation for extensive necrosis of the tibia the constrictor was applied just above the knee, and as soon as the patient recovered consciousness it became evident that the constriction had resulted in paralysis of the peroneal nerve. More than four months elapsed before function was completely restored. Since that time I always apply the constrictor higher up, where the nerves are protected by a thick cushion of muscular tissue, and have seen no more evil effects from elastic constriction of the lower extremity. Wherever it is safe to make the incision in the line of one or more fistulous openings this should be done, but when these are in localities where there would be danger of wounding important vessels, muscles, or nerves, another location must be chosen. In operations upon the humerus the exact location of the musculo-spiral nerve must be remembered, and if the incision necessarily comes close to this structure the dissection is made slowly and with the use of blunt instruments until the nerve is found, when it can be held out of the way. In operations upon the lower end of the femur, even if the fistulous opening should be in the popliteal space, the incision down to the bone should be made in the course of the intermuscular septum, on the outer or inner side, as the posterior surface of the femur can be made accessible from either side by making the incision large and by keeping close to the bone, separating the soft tissues well and keeping them out of the way by the use of retractors. Where the bone is covered by thick layers of muscles the incision is made in the direction of the muscles, and at a point corresponding to an intermuscular septum. The external incision should always be large, so as to afford plenty of space. As soon as the intermuscular septum is reached the scalpel should be laid aside and the parts carefully separated down to the bone by using the fingers or blunt instruments. When the bone is reached the periosteum is incised and reflected with the soft tissues attached to it. The opening of the involucrum is done with the chisel. In old-standing cases the involucrum is as dense as ivory and the chiseling is an exceedingly slow and laborious process, as only very small chips can be removed with each cut of the chisel. The brittleness of the new bone should warn the surgeon to chisel with care, as, otherwise, a fracture might result. If the chiseling is done at the site of a former opening, this opening is enlarged until the sequestrum is reached and can be extracted. Extraction of the sequestrum was the sole object of operations in the past; hence the dead bone was removed through a comparatively small opening in the bone, either *in toto* or after fragmentation. Modern surgery not only seeks to remove the dead bone, but to place the cavity in the best possible position for rapid healing. The first indication to be fulfilled in securing a favorable reparative process after the operation is to obtain an aseptic condition of the cavity. This can only be done by exposing the interior of the entire cavity. Chiseling is continued until both ends of the cavity are reached, when the sequestrum can be lifted out and the granulations lining the cavity are scraped out with a sharp spoon. Spoons of different sizes should be at hand, as the interior of such cavities usually present depressions and sinuses, which can be only dealt with successfully by keeping on hand different-sized spoons. After the mechanical removal of the infected tissues the cavity is washed out with a solution of corrosive sublimate (1 to 1000) and rubbed out and dried with an antiseptic sponge. It is evident that the healing of such a cavity, by unaided resources of nature, would be a slow process. Various attempts have been made to overcome the difficulties in the healing of cavities with unyielding walls. D. J. Hamilton suggested sponge-grafting. Neuber made flaps of the skin from each side, which he fastened to the floor of the cavity with bone nails.

Schede utilized the blood, which he allowed to accumulate in the cavity after suturing the external parts, and obtained some excellent results with this treatment. Recently, E. Hahn advised to detach the skin on each side to within an inch, at the posterior surface of the limb, for the purpose of better immobilization of the flaps, which are to be mitted over the centre of the gutter by suturing. For some years the author has been experimenting on animals with decalcified bone in the healing of aseptic bone-cavities, and the experimental as well as the clinical results obtained so far exceed all expectations. The decalcified bone-chips are preserved in an alcoholic solution of corrosive sublimate (1 to 500) or a solution of iodoform in sulphuric ether. The most essential condition for success, in the treatment of bone defects by implantation of decalcified bone, is a perfectly aseptic condition of the tissue to be brought in contact with the implanted bone. This condition is easily procured in operations on bones for lesions other than those caused by infection with pus-microbes, such as tumors, echinococcous cysts, and tuberculous and syphilitic affections uncomplicated by suppuration. In the surgical treatment of these affections, after the removal of the diseased tissue the seat of operation must be aseptic, if the ordinary precautions in the prevention of infection from without have been observed. In such cases speedy healing of the external wound and the early partial or complete reproduction of the lost bone are assured. The next most favorable cases for this procedure are circumscribed osteomyelitic processes in the epiphyseal extremities of the long bones, as we observe them in cases of primary circumscribed epiphyseal osteomyelitis, or in the form of a recurring attack in the same place, perhaps years after a diffuse osteomyelitis of the entire shaft. This method of treating bone-cavities is also applicable after operations for necrosis resulting from a previous attack of acute suppurative osteomyelitis. The cavity must be prepared for the implantation of decalcified bone in the manner described above. The implantation is made before the removal of the constrictor, in order that, after this is done, sufficient blood will escape to fill the spaces between the chips, and thus serve the useful purpose of a temporary cement-substance. After the cavity has been dusted over lightly with iodoform, the chips, which have been washed previously in an antiseptic solution, are dried upon a gauze compress, and are then poured into the cavity until this is packed with them as far as the periosteum. The first advantage derived from this method of bone-packing is that the chips serve as an antiseptic tampon which arrests the free oozing from the surface of the bone, which always takes place after the removal of the constrictor. Some blood escapes between the bone-chips and coagulates at once, thus forming a desirable and useful cement-substance which permeates the entire packing, and temporarily glues, as it were, the chips together and the entire mass to the surrounding tissues. The periosteum should be carefully preserved in exposing the bone, and, after implantation, is sutured over the surface of the bone-chips with absorbable aseptic buried sutures. If the bone is deeply located, it may become necessary to apply a second and third row of buried sutures in bringing into accurate apposition other soft parts. The skin is finally sutured with silk. It is of the greatest importance to secure accurate apposition of the divided soft parts, in order to preserve for the subjacent bone all of its natural coverings. In some instances it would be, undoubtedly, superfluous to secure any form of drainage, as, when the cavity is perfectly aseptic and hæmorrhage is not in excess of requirements, healing of the entire wound would be accomplished under one dressing. Experience, however, has taught me that tension arising from extravasation of blood often exerts an injurious influence upon the process of healing, and should be carefully avoided. As it is desirable to heal as much of the wound as possible without interfering with drainage, an absorbable capillary drain should be inserted in the lower angle of the wound. A string of catgut twisted into a small cord answers an admirable purpose. The wound is covered with a strip of aseptic protective silk, over which a few layers of iodoform gauze are applied. Over this a cushion of sublimated moss is placed, with a thick layer of salicylated cotton along its margins for the purpose of guarding more securely against the entrance of unfiltered air. The whole of the dressing is retained by a circular gauze bandage, evenly and smoothly applied. For the purpose of securing absolute rest for the limb, it is placed upon a posterior splint and kept in a slightly elevated position. If no indications arise, the first dressing is not removed for two weeks, when the entire wound will usually be found healed, except a few granulations at the place where the catgut drain was inserted. A smaller antiseptic compress is applied and the limb dressed in a similar manner. It is prudent to enforce rest,—not only till the external wound has healed, but until the process of repair in the interior of the bone has been completed, which embraces a period varying from four weeks to three months, according to the size of the cavity and the age of the patient. If an operation for necrosis with implantation of decalcified antiseptic bone-chips is followed by suppuration, it is an evidence that antisepsis was imperfect, and such cases must be treated upon the same principles as suppuration in other localities. If suppuration take place soon after the operation, and is profuse, it is probable that all of the bone-chips will have to be removed in order to facilitate the disinfection of the cavity. If it develop after granulation tissue has had time to form, and the discharge of pus is moderate in quantity, the prospects are that the bone will remain and serve its purpose as a nidus for the granulation tissue. In such cases an antiseptic irrigation should be made every three or four days until suppuration has ceased. If the bone-chips are lost by suppuration, or have to be removed for the purpose of a more thorough disinfection of the cavity, no attempt should be made at re-implantation until suppuration has been arrested; or, in other words, until the cavity has become lined with granulations, and is in a comparatively aseptic condition (when the time for secondary implantation has arrived). After the cavity has been irrigated with a strong antiseptic solution the superficial granulations are removed with a sharp spoon, and it is packed with bone-chips, which are implanted in the same manner as in the treatment of a recent cavity.

Complete closure of the external wound under these circumstances is seldom obtainable, and the surface of the exposed portion of the cavity should be provided with a thin layer of Schede's moist blood-clot. I have resorted to implantation of decalcified antiseptic bone-chips in the treatment of bone-cavities, after necrotomy and operations for tuberculosis of bone, in at least 25 cases, and have had the satisfaction of healing large defects without a drop of pus under one or two dressings in from two to four weeks. Only in a small percentage of the cases was it found necessary to remove the packing, and in most of these secondary implantation proved successful. Schede's blood-clot does not possess any antiseptic properties, like the bone-chips, and is not as permanent a structure. Operations by Neuber's method are often followed by necrosis of the flaps, and even if successful the lost bone is not restored. Implantation of decalcified antiseptic bone-chips, in the treatment of aseptic bone-cavities, is preferable to the use of viable grafts, as the substance used is not only absolutely aseptic, but possesses also valuable antiseptic properties, which must be looked upon as a valuable and important quality in the treatment of such cases. Reproduction of bone follows almost to perfection in every case where antisepsis proves successful; hence they serve the same purpose as viable grafts, as far as the restoration of lost tissue is concerned. I have chiseled a wide gutter in the humerus and tibia almost from one epiphysis to the other, for the removal of large sequestra, and have seen such enormous defects restored after implantation with bone-chips in a few weeks. The contour of the bone is restored to such perfection that after a few months it would be difficult to tell where the operation was performed. The bone-chips serve as a temporary scaffolding for the granulations springing from all sides of the bone-cavity, and as they are removed by absorption their place is occupied by living permanent tissue; first by embryonal cells, which are later converted into bone.

CHRONIC CIRCUMSCRIBED SUPPURATIVE OSTEOMYELITIS.

This is the bone-abscess of the older authors. The etiology of this form of suppurative inflammation is the same as in the diffuse variety. Clinically, two kinds can be distinguished: 1. Primary epiphyseal circumscribed osteomyelitis. 2. Secondary circumscribed osteomyelitis. The first kind is occasionally met with as a multiple affection, and is then attended by more or less constitutional disturbances and may result in epiphyseolysis. The secondary form occurs in bones that have been the seat of an attack of diffuse suppurative osteomyelitis, the patient apparently having recovered completely from the primary attack years before. It is still a question under discussion, if in these cases the infection is caused by microbes which have remained in the tissues in a latent state since the primary attack, or whether it is caused by localization of pus-microbes in the tissues weakened by the first attack. Rosenbach is of the opinion that recurring attacks of osteomyelitis in the same bone are caused by pus-microbes which have remained in the tissues, and which again become pathogenic when the tissues around them are rendered susceptible to their action by subsequent causes. I am strongly inclined to the same opinion. I have seen numerous cases where, in persons from 16 to 25 years of age, repeated attacks of circumscribed osteomyelitis occurred in a bone which, during childhood, had passed through an attack of acute osteomyelitis. The tibia, femur, and humerus are the bones which are most frequently attacked by recurrent osteomyelitis. The secondary attacks occur either in the centre of the sclerosed bone, the former site of the infected medullary cavity, or near one of the epiphyseal lines. I have no doubt that secondary osteomyelitis will be of less frequent occurrence after early operations for osteomyelitis, and that antiseptic sequestrotomy will be more generally practiced.

Symptoms.—The most important symptoms of circumscribed central suppuration in bone are pain and tenderness. The pain is deep-seated, intense, of a boring or gnawing character, and is generally more severe after active exercise and during the night. It is often intermittent, and has frequently been wrongly interpreted as neuralgia of bone.

The tenderness is circumscribed, and corresponds to the location of the suppurating focus. It is due to a circumscribed secondary plastic periostitis. The external swelling is slight, and often completely wanting. Usually neither redness nor œdema are present.

Pathological Anatomy.—Limited suppurative osteomyelitis gives rise to a circumscribed abscess, which varies in size from a pea to a walnut. Necrosis of bone seldom takes place; if it does, the sequestra are small and composed exclusively of cancellated tissue. If the abscess is situated in an epiphysis it may open into the adjacent joint and become the cause of a secondary suppurative arthritis. Thrombo-phlebitis, sepsis, and pyæmia rarely occur. The periostitis which attends chronic suppuration in bone always assumes a plastic type, as the periosteum is beyond the reach of pus-microbes. Epiphyseal osteomyelitis is often associated with chondritis and osteoporosis,—conditions which may result in pathological fracture. If in this form of osteomyelitis the suppuration extend to the periosteum, a circumscribed suppurative periostitis occurs, which is followed by the formation of small abscesses in the epiphyseal region. Limited necrosis in these cases is of frequent occurrence.

Treatment.—Circumscribed osteomyelitic processes in the epiphyseal extremities of the long bones, as we observe them in cases of primary circumscribed suppuration in the epiphyseal region, or in the form of a recurring attack in the same place or in the sclerosed shaft, perhaps years after a diffuse osteomyelitis of the entire shaft, are favorable cases for implantation of decalcified antiseptic bone-chips, as an aseptic condition of the cavity can be readily procured after the operative removal of the infected tissues. The inflammatory focus can be located externally with accuracy by the presence of a circumscribed area of tenderness, and the centre of the tender spot constitutes the guide in the search for the abscess. The operation is performed under st [illegible] precautions, and by the bloodless method. The chiseling is done in the direction of the centre of the bone by making a track perhaps an inch square. If the abscess is not found at a certain depth the surrounding tissue is explored with a small drill, in different directions from the track, until it is discovered, when further excavation is again made with the chisel. As soon as the abscess has been fully exposed the pus is washed out, and the size of the cavity ascertained by probing. As the abscess is often surrounded by a zone of tissue infiltrated with pus, all of the infected tissues are scraped out thoroughly with a sharp spoon; after which the cavity is prepared for the implantation of the bone-chips in the same manner as in operations for necrosis. Iodoformization of the cavity and the implantation of antiseptic bone-chips are measures which are well calculated to resist the pathogenic action of pus-microbes which might still remain, and in the majority of cases will secure an aseptic healing of the wound. I have repeatedly seen cavities the size of a small orange, in the head of the tibia, heal under two dressings, with perfect restoration of the bone removed by this method of treatment. The means resorted to to obtain an aseptic condition of the cavity will often result in increase to twice its original size, but the loss of tissue is not to be taken into consideration when a method of treatment is to be employed which requires perfect asepsis in order to be successful in placing the parts in a condition where perfect restoration will be accomplished with almost unfailing certainty.

CHAPTER XI.

SUPPURATION IN LARGE CAVITIES; ABSCESS OF INTERNAL ORGANS.

THE suppurative affections of the different large cavities in the body present so many features common to all of them that they will be considered together in this chapter. Suppurative inflammation of a membrane, synovial or serous, lining a closed cavity, is characterized by the rapidity with which the inflammatory process spreads over the entire surface, and the retention of the products of inflammation in a preformed closed space. Abscesses of internal organs result from infection by the extension of a suppurative lesion from the surface along the course of blood-vessels, lymphatics, nerve-sheaths, or by localization of pus-microbes floating in the blood in a *locus minoris resistentiæ* of an organ.

SUPPURATIVE ARTHRITIS.

Suppurative inflammation in an intact joint is always caused by localization of pus-microbes in the synovial membrane, conveyed to this structure by the blood, which results in suppurative synovitis, and, by the extension of the infection to the other structures of the joint, is often followed by complete disorganization of the joint. In this manner metastatic suppurative synovitis is caused, as it occurs, in pyæmia, gonorrhœa, and in some of the general infective diseases.

Bacteriological Researches.—In animals susceptible to the action of pus-microbes, the injection into a joint of a pure culture is usually followed by acute suppuration, and, not infrequently, by the formation of extensive para-articular abscesses. Hoffa, Kranzfeld, and Krause have studied, with special care, the microbic origin of suppurative synovitis, and all of them found in the pus one or more varieties of the microbe of suppuration. Krause found, in the pus of suppurating joints in small children, a streptococcus, the identity of which with the one described by Rosenbach was proved by cultivation experiments. In one case the same microbe was also found in the products of a purulent meningitis, which followed in the course of the joint disease. The same streptococcus was found by Heuber and Bahrdt in pus from a suppurating joint, and in the diphtheritic membranes of a scarlet-fever patient. The so-called gonorrhœal rheumatism is a suppurative synovitis, but opinions are divided in reference to the pyogenic properties of the gonococcus. This microbe was discovered in gonorrhœal pus by Neisser, in 1879. Its direct etiological relation to gonorrhœa has been sufficiently demonstrated by experimental research and clinical observation. The gonococcus always occurs in pairs, and is, therefore, a diplococcus.

The cocci appear as hemispherical bodies, with their flattened surfaces in apposition, which imparts to the microbe the characteristic biscuit-shaped appearance. They are found in clusters upon, or, what is more probable, as Bumm asserts, within the pus-corpuscles of gonorrhœal pus. Their intra-cellular location was shown by Bumm, by examining pus-corpuscles in water; when, after imbibition of fluid, the cells became swollen, the cocci could be seen between the molecular granules of the protoplasm. The microbes within the corpuscles may become so numerous as to fill the entire space, with the exception of the nucleus. It can be cultivated upon solidified blood-serum, or agar-agar-meat peptone. Its pus-producing property in specific inflammation of the mucous membrane of the urinary organs and conjunctiva is well known, and at present is not attributed to its direct effect on the tissues, but to the action of ptomaines, which it produces. A number of cases have been reported which appear to show that under certain circumstances the microbe enters the circulation and becomes the cause of metastatic suppuration, especially in joints. Schwarz asserts that the gonococcus is constantly found in the effusion of joints in gonorrhœal rheumatism, in other abscesses caused by gonorrhœa, and in the glands of Bartholin, in women who have passed through an attack of gonorrhœa. Petrone detected the gonococcus in the effusion of joints and in the blood, in two patients suffering from gonorrhœal rheumatism. He regards the joint complications as metastatic processes caused by the gonorrhœal infection. Other authors found metastatic abscesses in gonorrhœal patients, cultivated from the pus-microbes of suppuration, and on this account regard them as the result of a secondary or mixed infection. If gonococci can transform epithelial cells of the urethra or conjunctiva into pus-corpuscles, there is no reason to doubt that under favorable

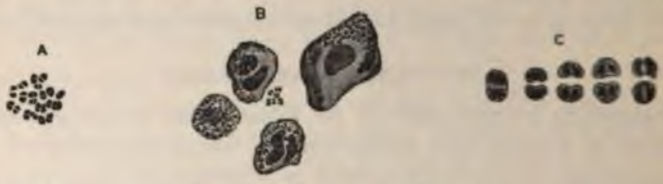

FIG. 61.—GONOCOCCUS. (*Bumm.*)

A. From a pure culture. B. From a blennorrhœic conjunctival secretion; an epithelial cell covered with cocci; a pus-corpuscle with cocci in the protoplasm; a pus-corpuscle completely filled with cocci; a free mass of cocci in close proximity to a pus-corpuscle. C. Development of gonococci.

circumstances they can exercise the same pathogenic effect on other tissues, particularly the synovial membrane of joints.

Symptoms and Diagnosis.—Suppurative arthritis is usually attended by a great deal of pain. This symptom is a prominent one in this affection on account of the intensity of the inflammation, and also because the pus accumulates with great rapidity in the joint, causing tension. Nocturnal exacerbations are common. The pain is greatly aggravated by passive motion, and any attempt on the part of the patient to use the joint vastly increases the suffering. Flexion of the joint is an early symptom, and increases in degree with the progress of the disease. In suppurative inflammation of the hip- and knee- joint it is not uncommon to find the limb flexed at right angles. In advanced cases of suppurative gonitis the tibia becomes partially dislocated backward and rotated outward. The swelling, as long as it is caused by the effusion into the joint, is proportionate to the amount of fluid contained in the joint. In the knee-joint the patella is raised from the condyles of the femur, the depressions on each side of it are effaced, and the upper recesses of the synovial sac become prominent. After perforation of the capsule, the pus escapes into the loose para-articular connective tissue, where it causes a rapidly-spreading phlegmonous inflammation. In very acute cases rupture of the capsule and an extensive para-articular abscess may appear in less than a week. With the rupture of the capsule of the joint the pain is diminished, but the general symptoms are aggravated. The parts around a suppurating joint usually present an œdematous appearance. The clinical history is often of great value in arriving at a conclusion in reference to the character of the synovitis. If an arthritis develop insidiously in connection with a suppurating lesion, attended by grave general symptoms, it is an evidence which renders a diagnosis of pyæmia more than probable. In pyæmia the joint affections appear often, either simultaneously or in rapid succession, as multiple affections. An obstinate joint affection, appearing in the course of an attack of gonorrhœa, is generally either a sero-purulent or suppurative synovitis. Gonorrhœal synovitis develops most frequently from the second to the fourth week after the appearance of the primary disease. If any doubt exist as to the character of the effusion into a joint, this can be readily dispelled by making an exploratory puncture with an ordinary hypodermic needle.

Treatment.—The only form of suppurative synovitis amenable to any other treatment, short of free incision, drainage, and antiseptic irrigation, is the sero-purulent effusion complicating gonorrhœa. In such cases aspiration, followed by compression of the joint and fixation of the limb in an immovable dressing, is usually successful in permanently removing the effusion. The absorption of the products of inflammation and return of function are hastened by massage and hot and cold douches. If a joint contain pus, temporizing measures should be abandoned, and the pus should be evacuated either by aspiration followed by washing out with an antiseptic solution, which should be repeated until the fluid returns clear, or, what is preferable in the vast majority of cases, the joint is treated from the beginning as an ordinary abscess. For irrigation of a suppurating joint with the aspirator, a ½-per-cent. (.5 per cent.) solution of acetate of aluminum should be used. The greatest care must be exercised not to inject atmospheric air into the joint, as, aside from the danger of increasing the infection by the admission of air, such accidents have been followed by immediate death from air embolism. The most efficient treatment in cases of suppurative arthritis is incision and drainage under strictest antiseptic precautions. As in the treatment of acute abscesses, the incisions must be made in places where drainage is most required. A long pair of hæmostatic forceps is an indispensable instrument in draining a joint. In draining the knee-joint three transverse tubular drains should be inserted, one beneath the tendon of the patella, one under the patella, and one across the upper recess of the joint. The fourth drain should be passed directly through the joint between the condyles of the femur, reaching from one side of the patella into the popliteal space. This would require eight incisions, each from ½ to 1 inch in length; half of them serve as openings into the joint for the forceps, while in making the remaining incisions only the skin and fascia are cut to the requisite extent over the point of the forceps. In tunneling the soft tissues in the popliteal space, with the forceps, from within outward, the opening is to be made to one side of the large vessels and nerves. Such an operation requires the administration of an anæsthetic and the use of elastic constriction of the limb.

As soon as all the drains are inserted the joint is washed out in different directions with one of the stronger antiseptic solutions, after which a copious antiseptic dressing is applied and the limb is immobilized upon a splint. If on the following day the fever has not subsided, or as soon as the dressing has become saturated with the discharges, it is removed, and the irrigation repeated as before. As soon as suppuration diminishes, through drainage is dispensed with and the drains are shortened from time to time, to be entirely removed with the disappearance of the swelling and the cessation of suppuration. The elbow-joint can be efficiently drained by passing a drain transversely through the joint, between the articular surfaces of the humerus, radius, and ulna. In draining the ankle-joint, a small incision is made down into the joint, at a point corresponding to the anterior margin of the external malleolus, through which a hæmostatic forceps is introduced and pushed in a backward direction, along the upper surface of the astragalus, until its point can be felt posteriorly under the skin, to the outer side of the tendo Achillis. The skin is then incised, the opening enlarged by unlocking the forceps and separating its blades, and a fenestrated rubber drain drawn through. If, as it so often happens, the posterior portion of the capsule of the joint bulge considerably, this can be drained by a drain inserted transversely underneath the tendo Achillis, near its attachment to the os calcis. Through drainage of the shoulder-joint in an antero-posterior direction can be established in the same manner without much difficulty. Drainage of the hip-joint is always difficult and never efficient. The best plan to follow is to open the joint from behind through an incision three or four inches in length, and then to pass a long pair of Pean's or polypus forceps between the capsule and the neck of the femur, either along the upper or lower border, in the direction of the groin, and to make a counter-incision upon the point of the instrument, and to draw a tubular drain through the whole length of the track. The wrist-joint can be drained transversely and antero-posteriorly, without fear of injuring any important structures. If suppuration continue, in spite of free drainage and careful antiseptic after-treatment, threatening the life of the patient from exhaustion or sepsis, more aggressive measures are indicated. Under such circumstances, it becomes often an exceedingly difficult matter to decide which one of the operative procedures should be adopted,—arthrectomy, excision, or amputation. If the patient's strength is so much reduced that arthrectomy or excision offer no prospects of a successful issue, amputation should be performed. This alternative becomes an unavoidable necessity if the suppurative arthritis is complicated by extensive burrowing of pus among the muscles, tendons, and para-articular tissues. If the patient's strength warrant an arthrectomy, this operation should be done if the disease is limited to the synovial membrane of the joint. Typical or atypical resection is to be restricted to cases where the articular cartilages and bone itself are found diseased. In resection of joints for suppurative affections, the surgeon must aim to remove only infected tissues; hence incomplete atypical are more frequently indicated than complete or typical resections. All cases of suppurative inflammation of joints should be treated from the beginning by immobilization of the limb and by the use of an appropriate mechanical support, both for the purpose of securing rest and to prevent deformities.

ENDOCRANIAL SUPPURATION.

(a) **Suppurative Pachymeningitis.**—Suppurative inflammation of the dura mater occurs either as a circumscribed or diffuse affection. It is caused by direct or indirect infection with pus-microbes. Direct infection occurs when the membrane is in communication with an infected penetrating wound of the skull. Traumatism, without infection, never results in suppurative inflammation of the envelopes of the brain; nor does the presence of an aseptic foreign body produce it. Aseptic injuries of the brain and its envelopes are productive of circumscribed, degenerative, or plastic lesions, but no suppuration. Septic inflammation of these structures, on the other hand, is noted for its tendency to become diffuse and to extend from one tissue to another, both by continuity and contiguity. Thus, in cases of pachymeningitis with loss of continuity of the dura mater, in cases of compound fractures of the skull, resulting from infection with pus-microbes from without, the inflammation commences upon the outer surface of the membrane, and if the pus-microbes do not penetrate the tissues the suppurative process remains superficial; but, as is more frequently the case, the microbes wander deeper into the tissues, until the entire thickness of the dura has become infected, and when the inner surface is affected, the underlying membranes, the arachnoid and pia mater, as well as the surface of the brain itself, are liable to become involved, step by step, by the extension of the infection from membrane to membrane and surface to surface. Suppurative pachymeningitis may remain as a circumscribed affection, and, if the internal surface of the dura is the seat of suppuration, it results in the formation of a subdural abscess. In circumscribed subdural suppuration, the diffusion of the pus between the dura mater and the arachnoid is prevented by a plastic exudation, which cements the two membranes together. In suppurative pachymeningitis, affecting only the inner surface of the dura, we often find a subcranial abscess, the outer wall of which is formed by the skull and the inner by the dura mater. The mechanical effect of the presence of pus in either locality will give rise to the same group of cerebral symptoms. Indirect infection of the dura mater with pus-microbes occurs in cases of suppuration in the epicranial tissues and in suppurative osteomyelitis of the cranial bones, by extension of the infection along the course of blood-vessels. In this way an insignificant peripheral suppurative lesion of the coverings of the skull is often followed by a grave form of endocranial suppuration.

Symptoms and Diagnosis.—Diffuse septic pachymeningitis is always attended by inflammation of the arachnoid, pia mater, and cortex of the brain, and the symptoms point more toward a cortical encephalitis than a pachymeningitis. Localized suppurative pachymeningitis gives rise to sy[illegible]ich indicate the presence of a phlegmonous inflammation, [illegible]is instance by symptoms arising from mechanical disturbances, caused by the presence of inflammatory exudation, or the participation of the surface of the brain in the suppurative process. In the acute septic form, following a compound fracture of the skull, the first symptoms are observed, usually, during the second or third day after the injury, and rapidly increase in intensity from the progressive extension of the infection. In the circumscribed form the symptoms are more localized. The headache is often severe, especially if the inflammation is located upon the inner surface of an intact dura, and involves a corresponding extent of the subjacent membranes and cortex of the brain. The early symptoms are those of irritation, to be followed, as the accumulation of pus increases, by evidences of compression. By means of focal symptoms it is often possible to locate the seat of the inflammatory product in the interior of an intact skull with sufficient accuracy to enable the surgeon to evacuate the pus by operative measures. Acute suppuration between the surface of the brain and the inner surface of the skull is always attended by a rise in the temperature. The pulse is accelerated, at first full and bounding, to become slower and slower as compression increases. If the pulse, in a case of endocranial inflammation, has been gradually reduced from 120 to 35 or 40, it is a sign that cerebral compression has reached the maximum extent compatible with life, and when it again reaches its former frequency it is an indication that dissolution is near at hand. The condition of the dura mater in subdural suppuration is of great importance in determining the presence or absence of accumulation of pus. In compound fractures, with loss of bone-substance, the existence of a subdural abscess is indicated by bulging of the dura into the opening of the skull and absence of cerebral pulsations. In trephining the skull for a supposed endocranial abscess, the surgeon's duty is to explore the subdural space, or to incise the dura mater, if this membrane appear tense or bulge into the opening, and if cerebral pulsations cannot be seen or felt.

Treatment.—The successful prevention of endocranial infection by rigid antiseptic precautions in compound fractures of the skull and endocranial operations is one of the best arguments in support of the value of the antiseptic treatment of wounds. Intentional opening of the skull under strict antiseptic precautions is seldom followed by suppurative endocranial inflammation. Compound fractures of the skull without fatal injury to the brain, if treated by strict antiseptic measures soon after the receipt of the injury, generally result in recovery of the patient. The most important indication in the treatment of these cases is to prevent infection of the wound, and thus guard most effectively against the occurrence of endocranial suppuration.

In the treatment of compound fractures of the skull, correction of mechanical difficulties is nothing compared with the importance of carrying out full antiseptic precautions to prevent the fatal complications. Suppurative pachymeningitis is prevented by the same treatment which secures an ideal aseptic healing in wounds of other parts. The prophylactic treatment aims at obtaining for the external wound, the fractured bones, and the exposed spaces underneath them a perfectly aseptic condition. The entire head should be shaved and the scalp rendered aseptic, by washing it with warm water and potash-soap, to be followed with a solution of corrosive sublimate (1 to 1000), and, lastly, with sulphuric ether or alcohol. The wound of the pericranial tissues is enlarged sufficiently to admit of thorough disinfection of the crevices between the fragments. Blood-clots and other foreign substances are to be sought for and removed, as infection is often traceable to imperfect treatment in this regard. Loose fragments are removed and kept in a warm solution of corrosive sublimate until they are re-implanted. Depressed fragments are elevated, and the space between the bone and the dura disinfected. If the dura has been lacerated the disinfection is carried farther. Detached and contused brain-tissue is removed. All hæmorrhage is carefully arrested, and after the final irrigation the dura is sutured, and, if necessary, a capillary drain of aseptic catgut or horse-hair inserted.

In the majority of cases it is advisable to drain the external wound by the insertion of a tubular drain at the most dependent point. Retention of the antiseptic dressing is secured best by applying a few turns of a plaster-of-Paris bandage. If, in spite of thorough primary disinfection, asepsis is not secured, secondary disinfection is to be instituted at once. This requires that the superficial sutures are removed. Detached bone is not to be re-implanted a second time, for fear of renewed infection. The whole surface is now disinfected by filling every sinus and depression with peroxide of hydrogen After effervescence has ceased the fluid is washed away by irrigation with the ordinary antiseptic solutions. The peroxide of hydrogen will reach parts of the infected surface inaccessible to other antiseptic solutions. If any evidences, local or general, point to the existence of a beginning inflammation of the dura mater and the subjacent membranes, the deepest portions of the wound are subjected to thorough disinfection and tubular subdural drainage is established. If secondary disinfection prove unsuccessful the antiseptic dressing is to be removed and the moist antiseptic compress substituted, which is removed from time to time, when the deeper portions of the wound are cleansed by irrigation with an antiseptic solution.

An external suppurative pachymeningitis is treated in the same way as an infected compound fracture of the skull. If it follow a compound fracture, loose, detached bones are removed, and the whole suppurating surface is disinfected; after which, tubular drainage is established. If it follow a fissured fracture, a sufficiently large opening is made in the skull, to permit of free disinfection, and the accumulation of pus is prevented by the insertion of a tubular drain. Suppuration between the dura mater and the cranial vault in an intact skull is treated by making one or more openings in the skull for disinfection and drainage. A subdural abscess without fracture of the skull is to be accurately located by a systematic and accurate study of the clinical history of the case, and by reference to the etiology of the suppurative process, and the information thus obtained can usually be corroborated by focal symptoms which point to the exact location of the disease. The skull is opened with the chisel over the point where the abscess is suspected. If the dura bulge into the opening, is tense, and the pulsations of the brain cannot be felt, the surgeon may be almost sure that a subdural abscess is present, and confirms his suspicion by an exploratory puncture. If pus is found, the dura mater is incised, the cavity washed out with an antiseptic solution, and a tubular drain is inserted. A daily change of the dressing and washing out of the cavity with antiseptic solution are necessary until suppuration has nearly ceased; then the dressing is removed less frequently, and the drain is shortened as the cavity diminishes in size. If at the point where the abscess was localized the dura present no indications of subdural, intra-cranial pressure, but the surgeon feels sure otherwise of his diagnosis, it is justifiable to make a number of small exploratory punctures until he succeeds in locating the suppurating focus. If the abscess-cavity is large, and the first opening has been made at a point unfavorable to efficient drainage, it is advisable to imitate the example of Macewan, to make a counter-opening in the skull and dura at the most dependent point, and to maintain through drainage until suppuration ceases. A localized suppurative pachymeningitis, recognized in time, and located with sufficient accuracy to admit of radical treatment by operative measures, is an affection which the modern surgeon treats with every assurance of success.

(b) Suppurative Leptomeningitis.—Inflammation of the arachnoid, without implication of the pia mater and surface of the brain, never occurs, and on this account we no longer speak of inflammation of any of these structures as separate lesions, but substitute the term *leptomeningitis*, by which is meant inflammation of the two inner envelopes of the brain, combined with cortical encephalitis. The surface of the brain is supplied in part with blood-vessels from the pia mater, and this intimate vascular connection establishes an equally intimate pathological relationship between these two structures. A septic leptomeningitis is a diffuse inflammation of the arachnoid, pia mater, and cortex of the brain, caused by infection with pus-microbes, and which, in the absence of all tendencies to localization, proves fatal before well-marked suppuration has occurred. Etiologically and pathologically it resembles diffuse septic peritonitis. Examination of the contents of the skull reveals great vascularity, more or less serous transudation, and softening of the gray matter of the brain. Microscopical examination shows only a moderate emigration of the colorless corpuscles and the minute changes in the capillary vessels, which are characteristic of acute septic inflammation. Suppurative leptomeningitis is characterized by the presence of pus between and upon the membranes and upon the surface of the brain. Septic leptomeningitis always terminates in suppuration, if the life of the patient is sufficiently prolonged for emigration of leucocytes and their transformation into pus-corpuscles to occur. Septic leptomeningitis sometimes appears within a few hours after a perforating wound of the skull. Bergmann relates the case of a child where a convex meningitis could be diagnosticated four hours after an injury of the skull. König reports a case that came under his observation where well-marked symptoms of leptomeningitis followed ten hours after perforation of the skull with the point of a sword. The wound was examined outside of the hospital with instruments that had not been disinfected. Ten hours after the injury the patient commenced vomiting, and had a temperature of 39° C. The following day, wild delirium, strabismus divergens, and a temperature of 40° C. The second day, coma, rapid pulse, and death. The necropsy revealed diffuse septic leptomeningitis. The inflammatory product is found most abundant in the subarachnoid space. The effusion in this space is sometimes clear, raising the arachnoid; it contains, also, fibrin in flakes and membranes, or it presents the consistence and color of pus. Pus first appears along the course of blood-vessels in the pia in the shape of yellow streaks, which, when they become confluent, tend to considerable inflammatory thickening of the membrane. Pus may also appear in the ventricles by way of communication with the subarachnoideal spaces. On account of the absence of connective-tissue spaces, the inflammation of the surface of the brain remains superficial. If pus form here, it appears as small abscesses, which later may become confluent, causing superficial destruction of the brain-substance. If the surface of the brain is the seat of a contusion, suppurative encephalitis is more diffuse, and may lead to a diffuse acute abscess underneath the infected envelopes.

Besides wounds communicating with the atmosphere through which infection takes place, suppurative leptomeningitis, like pachymeningitis, can be caused by peripheral suppurative lesions, as phlegmonous inflammation of the soft tissues covering the skull, suppurative osteomyelitis of the cranial bones, and suppurative inflammation of the middle ear. In fractures at the base of the skull, infection frequently occurs through a ruptured tympanum, or through a wound of the soft parts in the nasopharynx communicating directly with the meninges.

Symptoms and Diagnosis.—The surgeon should be versed in the symptomatology of suppurative leptomeningitis, rather for the purpose of knowing when not to interfere, by operative procedure, in cases of endocranial suppurative lesions, than to risk his reputation in a fruitless attempt in operating for an incurable disease. Diffuse septic and suppurative leptomeningitis are fatal diseases, and the surgical treatments will in all probability always remain of a purely prophylactic character. The symptoms of leptomeningitis are always those of cortical encephalitis, from which it cannot be distinguished during life. The disease is often initiated by a chill, like phlegmonous inflammation in other localities, followed by high fever and other symptoms of septic intoxication. In other cases the chill is absent and the fever develops more insidiously. The rise of temperature, which is usually abrupt,—the thermometer after a few hours shows an increase to 39° or 40° C., and as a rule presents but slight variations,—is caused by the absorption of septic material from the infected and inflamed tissues. The intra-cranial pressure and fever give rise at once to symptoms which indicate the presence of cerebral irritation. Headache, morbid sensitiveness to external impressions, sleeplessness, restlessness, and psychical perturbation are some of the most constant and conspicuous early symptoms. If the patient fall into a short nap he starts up suddenly and behaves like a maniac. The pupils are usually contracted at first, but dilate as other symptoms of compression appear. Often they are unequal in size and respond only sluggishly to light. Localized general convulsions frequently attend the stage of irritation. Vomiting and constipation are among the early symptoms. Paralysis of definite muscular groups, according to Bergmann, indicates extension of the disease to the region of motor centres. The face is suffused, the conjunctivæ injected, and the pulsations of the carotid arteries increased. The pulse, at first increased in frequency, bounding and firm, becomes slower as cerebral compression advances. If, after its frequency has been reduced to 40 or 50 beats per minute, it again becomes rapid, it is a sure indication of approaching death.

If the disease develop in the course of a perforating wound of the skull, the increased intra-cranial pressure is manifested by bulging of the dura mater into the wound, or if the envelopes of the brain have been lacerated, by hernia of the brain. The prolapsed portion of the brain often sloughs, when putrefaction of the dead tissue occurs as an unavoidable result, and death from sepsis is hastened by such an occurrence. Bergmann has recently called the attention of the profession to the fact that leptomeningitis, affecting the convex surface of the brain, leads at once to paralysis of one extremity, or hemiplegia, by the extension of the disease to motor centres. Indications pointing to localized symptoms of central irritation can be explained by the same theory. Leptomeningitis at the base of the brain is not attended by any definite localized focal symptoms, and the retraction of the head takes place in consequence of the extension of the inflammation to the meninges of the spinal cord. Basilar meningitis in its advanced stage gives rise to a peculiar disturbance of respiration,—the Cheyne-Stokes phenomenon. With the appearance of compression of the brain the symptoms of central irritation subside and give place to the paralytic stage. The patient passes from a condition of listlessness gradually into a stupor, and finally into complete coma. With the appearance of monoplegia and hemiplegia some centres may be still in a condition of irritation, so that symptoms of irritation and paralysis may be manifested at the same time. During the paralytic stage the suffusion of the face disappears, the face is pallid, and the whole surface of the body covered with a clammy, cold perspiration; the pupils dilate and no longer respond to light; the pulse becomes small and rapid, and death is preceded by relaxation of all sphincter muscles.

Treatment.—The prophylactic treatment has for its object the prevention of infection through wounds communicating with the contents of the skull. Rigid antiseptic treatment of all compound fractures of the skull must be carried out in the most pedantic manner. Fractures of the base of the skull, communicating with the atmospheric air through a ruptured tympanum or through a lacerated wound in the naso-pharyngeal region, should be treated upon the same principles as a compound fracture of the vault of the cranium. If the tympanum has been ruptured the external meatus is thoroughly disinfected and packed loosely with iodoform gauze, over which a filter of salicylated cotton is applied. If the fracture communicate with a wound of the naso-pharyngeal region, disinfection is aimed at by using an antiseptic nasal douche and plugging the posterior nares with tampons of iodoform gauze, which are to be removed daily, and, after using the nasal douche, are to be replaced by new ones. The prophylactic treatment of leptomeningitis, caused by suppurating foci in the coverings of the skull, the internal ear, or in the cranial bones, can be carried out most successfully by early and rational treatment of the primary diseases. With the first appearance of the symptoms of leptomeningitis, the surgeon should lose no time in rendering the wound or primary suppurating depot aseptic by operative measures, combined with most rigid antiseptic precautions, with a faint hope that such measures may, in exceptional cases at least, lead to a successful issue by limiting the extension of the infection. As soon as the disease has become diffuse the prospects of a favorable termination are almost *nil*. It may be possible that multiple openings in the skull, with subarachnoid drainage and frequent antiseptie irrigations or permanent irrigation, will in the future become an established and feasible method of treatment in such cases. From a surgical stand-point such heroic treatment appears the only rational course to pursue in a class of patients otherwise doomed to certain death. The multiple perforations would have a potent influence in diminishing the intra-cranial pressure, and drainage, combined with frequent or permanent irrigation, might, at least in a small percentage of cases, succeed in sterilizing the extensive area of infection.

BRAIN-ABSCESS.

The term *abscess of the brain* should be limited to circumscribed collections of pus surrounded on all sides by brain-tissue. Suppuration occurring between the brain and its envelopes, from a circumscribed suppurative leptomeningitis, is not a brain-abscess. A brain-abscess is the result of a circumscribed suppurative encephalitis. The acute form occurs when a contused portion of the brain becomes infected through a wound communicating with the atmospheric air, but, as this form will seldom, if ever, become the subject of successful operative treatment, our remarks will apply to abscess of the brain proper, or chronic abscess. A chronic circumscribed encephalitis may originate in a contused area of the brain, without any external wound or direct route of infection, from localization of pus-microbes in the *locus minoris resistentiæ*. Such cases have been frequently observed where, weeks and months after the subsidence of the symptoms resulting from the immediate effects of a head injury, remote symptoms pointed to a central suppurating focus in the brain. The occurrence of such grave remote consequences renders the prognosis, even after slight injuries to the skull, always more or less doubtful. In other instances an abscess forms around a foreign body that has lodged in the brain, and has remained for a long time without having given rise to any local or general disturbance. Infected penetrating wounds of the skull may heal, and the patient apparently recover perfect health, when at some remote time, and in direct causal connection with the previous infection, a chronic abscess develops, perhaps, some distance from the primary seat of infection. Most frequently such abscesses are caused by suppurative inflammation of the internal ear, and suppurative osteomyelitis of the cranial bones. In size they vary from that of a pea to that of an entire hemisphere. They may remain stationary for twenty years, but the period of latency may pass into activity at any time. A large abscess in the white substance of a hemisphere may give rise to no functional disturbances whatever, and can only be recognized by the terminal symptoms. In other cases the abscess can not only be diagnosticated during life, but its location accurately determined by symptoms which point to destruction of a particular part of the brain.

Symptoms and Diagnosis.—The first symptoms are insidious in their onset, and often of a very indefinite nature. The first thing noticed is, frequently, a hypersensitiveness and irritable temper of the patient, with more or less severe headache. Early loss of memory is often noticed, and the patient becomes dull, sullen, unconcerned, and reckless in his business transactions. If the abscess involve any of the motor centres, or a considerable portion of fibres originating from them, monospasm or hemispasm, or monoplegia or hemiplegia follow as peripheral evidences of the central lesion. General convulsions, which sometimes occur at this stage, have less diagnostic value than localized focal symptoms. Abscess of the brain seldom causes fever; on the other hand, the temperature is often subnormal. A sudden rise in temperature indicates that the abscess has reached the surface of the brain, and that a terminal leptomeningitis has developed. Rupture of an abscess into one of the ventricles is followed by general convulsions, paralysis, and death. Prominence of the dura over the abscess and absence or diminution of cerebral pulsation are important diagnostic signs, especially in cases where the abscess is located near the surface of the brain. Examination of the exposed brain by palpation may elicit evidences of deep-seated fluctuation. In exceptional cases the portion of brain covering the abscess is firmer than normal from inflammatory infiltration (Rose).

Gussenbauer states that in some cases the presence of the abscess can be ascertained by the existence of fluctuation.

Prognosis.—An abscess in the brain is always an imminent source of danger to life. A considerable accumulation of pus in the brain, like in any other organ, is never removed by absorption. If the abscess remain in the active stage it gradually increases in size until it ruptures into one of the ventricles or reaches the surface of the brain, in either event resulting in complications which lead to a rapidly fatal termination. It may remain in a latent condition for an indefinite period of time, but the life of the patient is always in jeopardy, as acute exacerbations may come on at any time. If an abscess form after a perforating injury of the skull, and the pus finds an exit through a permanent fistulous opening, the general health may remain sufficiently good to enable the patient to follow his occupation. A case came recently under my observation where I could introduce the probe to a distance of four inches into the brain, and yet the general health remained unimpaired, although this condition had existed for years. The brain-abscess in this case developed in connection with purulent inflammation of the middle ear. I have knowledge of another case, where a young man received a perforating wound of the skull, which was followed by the formation of an abscess of the brain that discharged externally. The patient filled, in a creditable manner, a responsible and important government position for thirty years, and died from another cause.

The necropsy showed an abscess-cavity the size of an orange, located in the anterior right lobe of the brain, which communicated with the external surface through a fistulous opening in the skull. A few cases are reported where recovery followed the spontaneous discharge of the contents of the abscess through the ear or nose, but ordinarily such an occurrence is followed by putrefaction of the remaining contents of the abscess-cavity and death from sepsis.

Treatment.—All efforts to cure an abscess of the brain by external applications, or internal medication, will be worse than useless in effecting removal of the pus by absorption. All expectant treatment is worse than useless. Brain-abscess must be treated on the same principles as abscess in any other organ, by incision and drainage. The great difficulty in these cases is to make a sufficiently accurate diagnosis in regard to the exact location of the abscess. Before anything was known in reference to the subject of cerebral localization, Dupuytren plunged a bistoury deeply into the brain, and was fortunate enough to hit an abscess which he suspected, and his patient recovered. The same bold treatment has been frequently followed since, but not with the same brilliant result, as, in the majority of cases, either no abscess existed or the incision was made, not into, but aside of, the abscess. Renz cured an abscess of the brain by repeated aspirations through a fissure in the skull. The average surgeon, at the present time, would not undertake to incise a brain for abscess unless he had previously located the abscess by a careful study of focal symptoms, and by a resort to exploratory punctures. Bergmann condemns the use of the exploring-syringe for this purpose, but in the hands of those less skilled in cerebral localization than this eminent surgeon the exploring-needle will always be regarded as a welcome and useful instrument of exact diagnosis.

Cerebral Localization.—As the peripheral symptoms upon which the surgeon relies in locating an abscess in the brain are caused by irritation or destruction of the motor tracts or centres, it is absolutely necessary for him to become familiar with the topography of the motor centres. A. W. Hare gives a very practical instruction on cerebral localization in a paper published in the London *Lancet*, March 3, 1888, from which I will quote below:—

"In the parietal region, grouped around the fissure of Rolando, are the areas associated with movements of the extremities of the opposite side of the body, and, at the lower end of the fissure, those related to movements of the mouth and tongue. In the accompanying diagram (Fig. 62) the motor areas have been marked in their anatomical relations to the other structures of a normal head, dissected for the purpose, showing the brain in its natural position. The areas associated with movements in neighboring regions of the body have been shaded alike in the figure. Thus, the areas A, B, C, and D, bounding the fissure of Rolando posteriorly, and 5 and 6, in front of the fissure, together with 2, 3, and 4, at its upper end, are those in functional connection with the upper extremity; A, B, C, and D being concerned in the movements of the fingers, head, and wrist, 5 in a forward movement of the arm, 6 in pronation and supination of the forearm, and 2, 3, and 4 in co-ordinated movements of the whole upper extremity. The areas 7, 8, 9, 10, and 11, indicated as having a common region of motor representation, are related to movements of the tongue and of the muscles around the mouth. Area 1 represents in part movements of the lower extremity. In the same way areas of representation of general and of special sensation are located by Ferrier around the horizontal limb of the fissure of Sylvius. It must not be overlooked that this mapping out of areas has an absolute exactitude only in the case of the species of ape upon which the experiments were performed. Its bearing in the human subject is one of great

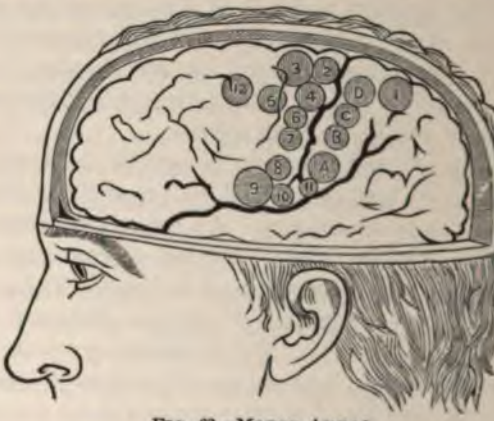

FIG. 62.—MOTOR AREAS.

relative importance, but it must not be looked upon as a final statement of fact, in the case of man, until each area can be shown to be correctly placed, as it is by the accumulation of a sufficient number of clinical and of post-mortem observations directly confirming the method employed.

"In the study of cranio-cerebral topography the surgeon has to rely on four primary landmarks in establishing a system of measurements. These are the glabella, or root of the nose, which bears a definite relation to the anterior limit of the cranial cavity, and the occipital protuberance, or inion, which bears a similar relation to its posterior end, corresponding to the junction of the falx with the tentorium. The whole mass of the cerebrum is disposed between these two points, and they bear definite relations to its cortical matter, uninfluenced by the structure and contour of the bones forming the vault. The third constant landmark is the external angular process of the frontal bone, which bears a relation to the lateral expansion of the frontal lobes, similar to that borne by the two prominences already mentioned, to the anterior and posterior extremities of the cerebrum. It has also a uniform relation to the fissure of Sylvius. Lastly, the parietal eminence is of value, since it marks the greatest lateral expansion of the substance of the hemisphere, and, as Turner has shown, bears a special relation to the submarginal convolution. To find the upper end of the fissure of Rolando by the use of these data, the surface measurement in the middle line of the head should be taken over the scalp from the glabella to the occipital protuberance. In ordinary adult heads this will vary from 11 to 13 inches; measured along this line from before backward, the distance from the glabella to the top of the fissure will be 55.7 per cent. of the total distance from the glabella to the occipital protuberance. The following scale shows the distance from the glabella to the top of the fissure in all ordinary heads:—

When the distance from the glabella to the occipital protuberance is	The distance from the glabella to the upper end of the fissure of Rolando is
11 inches,	6⅒ inches.
11½ "	6⅜ "
12 "	6⅝ "
12½ "	7 "
13 "	7⅛ "

"To find the top of the Rolandic fissure, Thane halves the distance from the glabella to the occipital protuberance, and, having thus defined the middle point of the vertex, takes a point half an inch behind it as the location of the upper end of the fissure. Having thus ascertained the upper end of the fissure, it is desirable to determine its length and direction. The scalp measurement corresponding to its length is

$3\frac{3}{4}$ inches. It runs from above downward and forward, its axis making an angle of 67 degrees with the middle line.

"Wilson's cyrtometer is an exceedingly useful aid in locating the fissure of Rolando. It consists of three strips of flexible metal and a tape for securing it *in situ*. The method of its application is illustrated by Fig. 64.

"The broadest, transverse strip passes coronally around the forehead, corresponding with the glabella and external angular process; the narrower, longitudinal strip passes backward from the glabella in the middle line to the occiput. This strip is marked with two scales of letters,—capitals in its posterior fourth, and small letters about the middle of the strip. These two scales bear a relation to one another, calculated to aid in the application of the instrument to an ordinary head. Measured from the glabella backward, the distance to any given small letter is 55.7 per cent. of the distance from the glabella to the corresponding capital letter; thus, when any capital letter will coincide with the top of the fissure, a third narrow, reversible strip strikes on the longitudinal strip of metal, marking an angle of 67 degrees, opening forward and marked at $3\frac{3}{4}$ inches from its attached end, thus giving the length and direction of the fissure on the surface of the head. To determine the exact location and direction of the fissure, a line is drawn

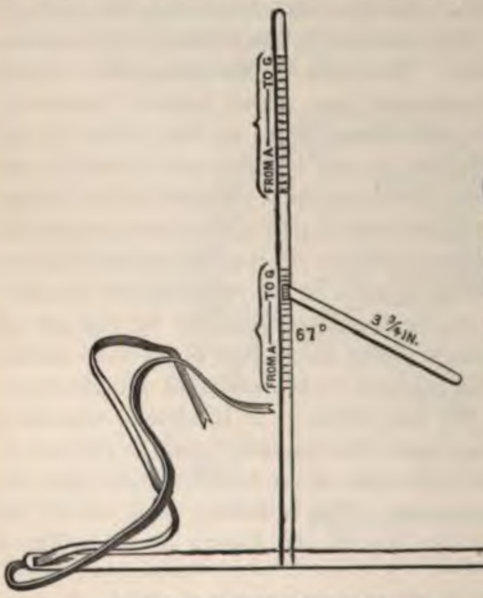

FIG. 63.—WILSON'S CYRTOMETER.

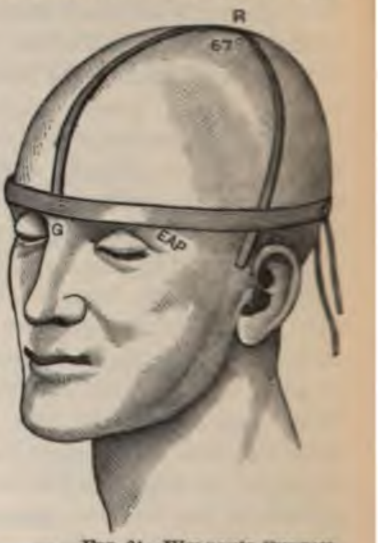

FIG. 64.—WILSON'S CYRTOMETER APPLIED.

G, glabella; E A P, external angular process; R, fissure of Rolando, its position and direction marked by the lateral strip of metal.

from the external angular process of the frontal bone backward to the occipital protuberance, taking the shortest route between these points. Such a line drops a little toward the external auditory meatus, avoiding the greater convexity of the skull, which lies in the course of a horizontal line between the bony prominences. It usually passes about ½ inch above the meatus, and thus closely corresponds to the floor of the middle fossa, and behind runs parallel to and nearly in the same course with the attachment of the tentorium and the posterior half of the lateral sinus. A measurement of 1⅛ inches along this line, backward from the external angular process, marks the lower end of the fissure of Sylvius. From this point a straight line drawn to the centre of the parietal eminence accurately marks the course of the posterior limb of the fissure. The main line of the fissure follows the line of the squamo-parietal suture to its highest point, whence it continues its course to the parietal eminence. The middle meningeal artery, after grooving the inner surface of the great wing of the sphenoid, passes on to the anterior angle of the parietal bone, and is distributed to the dura mater lining the anterior and superior half of the bone. If the surgeon desire to expose the tip of the temporo-sphenoidal lobe, he should open the skull

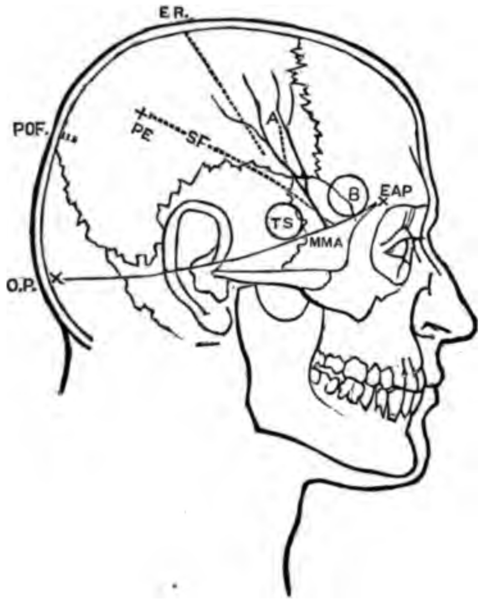

FIG. 65.—HEAD, SKULL, AND CEREBRAL FISSURES. (*Adapted from Marshall.*)

O P, occipital protuberance; E A P, external angular process; S F, Sylvian fissure; A, its ascending limb; F R, fissure of Rolando; P E, parietal eminence; M M A, middle meningeal artery· T S, tip of temporo-sphenoidal lobe; B, Broca's convolution.

behind the upper extremity of the great wing of the sphenoid; if to expose Broca's convolution, immediately in front of the same bony peninsula. The sites of the two operations are shown in Fig. 65."

Opening of the Skull.—The operative treatment of abscess of the brain presupposes an accurate diagnosis by means of cerebral localization and a careful study of the clinical and etiological aspects of the case. If symptoms of abscess of the brain arise, after a compound fracture of the skull, before the continuity of the skull has been restored, exploration can be done with a fine needle through a fissure, or at some point where fragments have been removed; and, if pus is found, a closed hæmostatic forceps can be pushed along the side of the needle into the abscess, and the track enlarged by separating the blades before withdrawing the instruments. Into this track a drainage-tube is introduced, the abscess-cavity gently irrigated, and the wound disinfected and dressed antiseptically; or, a small quantity of peroxide of hydrogen can be injected into the abscess-cavity through the drainage-tube, which will not only force out the contents, but will also sterilize the walls of the abscess more thoroughly than any other antiseptic. If an abscess develop in the brain in an intact skull, or after the fracture has healed, the skull must be opened at a point immediately over the abscess. By means of the measurements given, or by the use of Wilson's cyrtometer, the motor centre or centres affected by the abscess are marked upon the shaved and disinfected scalp before the skull is exposed; and the exact location of the abscess is also marked on the skull by making a puncture through the scalp with a small perforator, so that the location can be recognized after the soft parts have been reflected. The bone is laid bare at this point by Horsley's flap, which is made by a horse-shoe-shaped incision, the convexity of which is directed upward. The flap, with the periosteum attached, is turned downward. After all hæmorrhage has been arrested the skull is opened, either by using a large trephine or, what is better, with a chisel; the button of bone or bone-chips are transferred into a warm antiseptic solution, where they are kept until needed for re-implantation, should this be deemed necessary or advisable. If the dura mater is tense and bulge into the opening, and cerebral pulsations are feeble and entirely wanting, the indications are that the skull has been opened near or directly over the abscess. The opening need not be larger than an inch in diameter.

Methodical Exploration of the Brain.—Experiments and clinical experience have shown that the brain can be explored in different directions with a fine, hollow, aseptic needle without any immediate or remote bad effects. The brain should never be incised for abscess until the abscess has been located by methodical exploration. An ordinary exploring-syringe with a delicate needle about 4 inches in length should be used for this purpose. The needle is pushed into the brain in the direction in which the abscess is suspected, and to the necessary depth, when aspiration is made and the result carefully noted. If no pus is found the needle is withdrawn or pushed forward in the same direction, and aspiration made at different points in its track; and, if no pus is found in that direction, it is withdrawn and pushed in another direction, and the same manœuvres repeated. In this manner a large territory can be explored and even very small abscesses located. When the abscess has been located by this method of exploration, the needle is used as a guide for a small pair of hæmostatic forceps, which is pushed forward along its side until the abscess has been reached, when it is unlocked, the blades slightly separated, and as the instrument is withdrawn the track is sufficiently enlarged to permit the insertion of a rubber drain the size of an ordinary lead-pencil. The needle is only removed after the drain is *in situ*. Fenger, of Chicago, has written an exceedingly valuable paper on exploration of the brain, in the diagnosis and treatment of abscess of the brain, in which he has furnished abundant proof both of the harmlessness and utility of this procedure.

After the abscess has been opened and drained, it is advisable to wash it out gently with some non-irritating and yet effective antiseptic solution, either with half of a 1-per-cent. solution of acetate of aluminum or a 2-per-cent. solution of boracic acid, or it is injected with peroxide of hydrogen. As the abscess-walls are never firm, every precaution must be taken to prevent overdistention, but gentle irrigation is continued until the fluid returns clear. If the skull has been opened by removing a disk of bone by trephining, an opening in this must be made at its lower margin, which will permit bringing the drainage-tube out to the external surface after implantation. If bone-chips are re-implanted, a space for the drain must be left in the most dependent portion of the opening. The drainage-tube is brought out at one of the lower angles of the wound or through a button-hole in the flap. The flap is secured in its position by a requisite number of sutures. Daily changes of dressing is required until suppuration diminishes, when the drain is shortened from time to time and the dressing changed less frequently. The drainage-tube is not to be removed until the abscess-cavity is closed, as otherwise a relapse would be liable to occur which would require a repetition of the first operation. The most unsatisfactory aspect of the surgical treatment of abscess of the brain is the fact that in some instances multiple abscesses are present,—an occurrence which is beyond the limits of the present means of diagnosis. In such cases the surgeon may cure one abscess, but the patient succumbs from the effect of those that have not been discovered. The appearance of a *hernia cerebri*, after the evacuation and drainage of an abscess of the brain, is a condition which points to the existence of an additional abscess or abscesses. Should such a condition appear during the after-treatment of an abscess of the brain, treated by evacuation and drainage, it would furnish a strong temptation to resort to another methodical exploration with a view of subjecting additional abscesses to the same radical treatment. Should the first opening into an abscess of the brain not be suitable for effective drainage, it would be well to follow the example of Macewan and open the skull at a lower point, tunnel the intervening portion of the brain, between this opening and the abscess cavity, with hæmostatic forceps, and thus establish an additional and more efficient route for drainage. In the surgical treatment of abscess following suppurative inflammation of the middle ear, it is well to remember that in these cases the abscess is usually located in the vicinity of the petrous portion of the temporal bone, and that in exploring the brain the needle should be inserted in this direction.

EMPYEMA.

Empyema is a collection of pus in the pleural cavity. It is always the result of a suppurative pleuritis.

Bacteriological Studies.—A penetrating wound of the pleural cavity is more frequently followed by infection with pus-microbes and suppurative pleuritis than perforation of one of the bronchial tubes, as in the latter accident the atmospheric air entering the pleural cavity has undergone a process of filtration during its passage through the respiratory tract. Suppurative pleuritis, occurring without direct infection through a perforation in the thoracic wall or one of the bronchial tubes, is always caused by localization of pus-microbes within or upon the serous membrane lining the pleural cavity. Localization of pus-microbes occurs in the pleura or pleural cavity, either as a primary or secondary infection. Fränkel made a bacteriological study of 12 cases of empyema. In 3 cases, in which no special cause could be traced, the pus contained exclusively the streptococcus pyogenes. In 3 cases the pus contained only pneumococci. Other authors have found in such cases also other pus-microbes. Fränkel believes that when this is the case they have localized in consequence of a secondary invasion. The presence of streptococci in the pus from a suppurating pleural cavity presents nothing characteristic, as the microbe is also found in cases in which the empyema is secondary to pneumonia and tuberculosis. On the other hand, he assigns to the pneumococcus, in pus taken from a pleural cavity, a diagnostic significance, as it proves, beyond all doubt, that the suppurative pleuritis occurred in the course of a pneumonia as a secondary affection; consequently, its presence in the pus is positive proof that a pneumonia exists or has existed, even if the clinical and physical symptoms were not sufficiently clear to indicate its existence. In 4 cases the empyema had a tuberculous origin, in 2 of which pneumothorax was present at the same time. The presence of the bacillus of tuberculosis in the pus is not easily demonstrated, but the absence of this microbe is no sign that the disease is not tubercular, as inoculations with pus in animals almost constantly produce typical tuberculosis. In the pus of tubercular pyo-pneumothorax, if micro-organisms are present, the bacillus of tuberculosis can be found, and the pus shows no tendency to undergo putrefactive changes, in contradistinction to empyema occurring in non-tuberculous subjects, in whom spontaneous discharge through the bronchial tubes takes place. Senator maintains that putrefaction is prevented by the parenchyma of the lungs acting as a filter, preventing ingress of bacteria with the inspired air, and by the presence of a large amount of carbonic-acid gas in the air of the cavity, as it is well known that microbes do not thrive so well in such an atmosphere as in ordinary air. Ehrlich has made an interesting bacteriological examination of the pus in 19 cases of empyema; in only 7 of these could the bacillus of tuberculosis be found; in the remaining 12 this microbe could not be detected, and upon this negative ground the existence of tuberculosis was excluded. Further observation in these cases after operation corroborated the diagnosis. He asserts, therefore, that, in the purulent pleuritic exudation in tubercular patients in empyema and pyo-pneumothorax, the presence of the specific microbic cause can always be demonstrated. This author places the greatest importance on a bacteriological examination of the pus as a means of differential diagnosis between suppurative and tubercular empyema. A serous effusion is not infrequently transformed into an empyema by a change of the predominant bacteriological cause. In a number of cases I found it necessary to aspirate the chest for the removal of a copious effusion. The fluid removed at the first aspiration was clear serum; the second aspiration removed a slight, turbid fluid, and the third aspiration yielded a distinctly sero-purulent fluid; while the fourth aspiration revealed a well-marked empyema. In all of these cases the subsequent history and termination showed that tuberculosis was the primary cause of the effusion. Infection of the tubercular foci with pus-microbes, and the entrance of these into a cavity already changed by disease, altered the type of the inflammation and the character of the effusion. Putrefaction of the products of suppurative pleuritis occurs occasionally without the presence of a direct communication of the pleural cavity with the atmospheric air. I have seen 2 cases of this kind, and both recovered after radical operation. In such instances we must take it for granted that saprophytic bacilli find their way into the pleural cavity through the respiratory passages and the parenchyma of the lungs, and select the products of coagulation necrosis for their nutrient medium. The pus in such cases is exceedingly fetid, thin, and usually contains large shreds of fibrin. The ptomaines of the putrefactive bacteria increase the fever and other symptoms of septic intoxication.

Diagnosis.—The presence of a considerable quantity of fluid gives rise to well-marked clinical and physical symptoms. Aside from the ordinary symptoms which point to a suppurative inflammation in other localities, such as chill, fever, pain, loss of appetite, the patient complains of difficulty of breathing, especially on lying down, and sometimes, but not always, of a short, hacking cough. On physical examination it becomes apparent that a part or nearly the entire pleural cavity is occupied by a fluid. Dullness on percussion and absence of respiratory and voice sounds over the area occupied by the fluid, and displacement of adjacent organs by the intra-thoracic pressure, are signs which cannot be well simulated by anything else than accumulation of fluid in the pleural cavity. Bulging of intercostal spaces, as a rule, is more marked in empyema than hydrothorax. In empyema the subcutaneous tissues on the affected side are often slightly œdematous and the superficial veins are sometimes enlarged. In empyema of the right pleural cavity the liver is pushed in a downward direction, while the heart is displaced toward the left side. In empyema of the left side the apex-beat of the heart can quite frequently be felt on the right side of the sternum. A temperature of 100° to 101° F. in the morning and 101° to 103° F. in the evening, continued for several weeks, speaks strongly in favor of empyema. A positive diagnosis always rests on demonstrating the presence of pus in the pleural cavity, which can be done, without danger and without pain worth mentioning, by an exploratory puncture with an ordinary hypodermic needle. In puncturing the chest for exploratory or therapeutic purposes, it should be borne in mind that the needle should be inserted in a direction which corresponds to the centre of the intercostal space, consequently in an oblique direction from below upward. If no contra-indications present themselves, the exploratory puncture should be made at the place where, later, the radical operation will be performed; that is, in the axillary line, between the sixth and seventh or seventh and eighth ribs. If the needle is perfectly aseptic no harm will result, even should the lung or liver be punctured.

Prognosis.—Simple, uncomplicated suppurative pleuritis offers a favorable prognosis if subjected to early radical treatment. The prognosis is more favorable in children than in adults, and in recent than in old cases. In long-standing empyema the lung becomes atelectatic from compression, and its full expansion is also prohibited by numerous firm adhesions. In children, partial expansion of the lung is compensated for by retraction of the yielding chest-wall, enabling the pleural cavity to close; while, in the adult, incomplete expansion of the lung results in a physical condition which renders definitive healing a difficult, if not even an impossible, occurrence. Pulmonary tuberculosis complicated by empyema constitutes a contra-indication to radical operation, as the patient is already affected by a disease which almost necessarily leads to a fatal issue, and a radical operation would only hasten this termination.

A fistulous communication between a bronchial tube and the pleural cavity, resulting from a rupture of an empyema in this direction, in exceptional cases, leads to a spontaneous cure, but more frequently becomes a cause of retardation of recovery after an operation.

Treatment.—An empyema is nothing more nor less than an abscess in the pleural cavity, and should be treated as such. There can be no doubt that in exceptional instances a cure has been effected by aspiration. This method of treatment promises more in children than in adults, and it is also in the former that the radical operation has yielded the best results; hence it is not advisable to have recourse to an uncertain procedure if a radical operation accomplish the same result with greater certainty, more speedily, and with no greater immediate and remote risks to life. It is a good plan in every case to combine aspiration with exploration, for the purpose of improving the conditions for a radical operation. By aspiration we demonstrate the presence of pus in the pleural cavity, and, by removing the fluid completely or in part, we aid the expansion of the lung, which, by the time the radical operation is performed, has become adherent lower down. Aspiration is to be followed, in the course of two or three days, by a radical operation. By a radical operation we understand incision of the pleural cavity and draining the same. The operation for empyema by incision and drainage must always be done under the strictest antiseptic precautions, as any mistake or negligence in this regard is exceedingly liable to be followed by infection with putrefactive bacteria,—an occurrence which would greatly increase the danger from sepsis. Nothing but perfectly aseptic material must be used, and the whole chest of the patient and the hands of the operator must be thoroughly disinfected by washing with hot water and potash-soap, and disinfecting with a 1-to-1000 solution of sublimate, and finally with alcohol. The instruments must be boiled for at least ten minutes.

(a) Incisions.—If an empyema is perforating the chest-wall and appears as a subcutaneous abscess, the incision is made through the centre of the abscess and parallel to the ribs. If no such indication is present, the incision should be made over the centre of the sixth rib and parallel to it on the right side, and over the seventh on the left, at a point half-way between the nipple and the axillary line. It must be about 4 inches in length and extend down to the bone.

(b) **Resection of Rib.**—The soft parts, with the periosteum, are reflected with an elevator, which is then passed between the periosteum and rib, posteriorly, from below upward, and the periosteum separated to the extent of 1½ inches. If the elevator is kept in close contact with the bone, there is no danger of injuring the intercostal vessels or nerves, nor of opening the pleural cavity prematurely. With the elevator the rib is raised, and a section 1½ inches in length is removed with a pair of heavy bone-forceps. After the removal of the bone, all hæmorrhage is carefully checked. If the pleura feel tense and bulge into the wound, there is no necessity of making another exploratory puncture. If this is not the case, as a matter of precaution, another puncture can be made, at this stage of the operation, to satisfy the surgeon of the presence of pus underneath. The incision into the pleura is then made with a bistoury, in the centre of the periosteal gutter, through this membrane and the pleura, into the cavity of the chest. This incision must be large enough to allow the insertion of drainage-tubes the size of the little finger. The deep incision in the soft parts can be readily dilated to the requisite extent by the insertion of a finger, which may also be used in interrupting the flow.

(c) **Evacuation of Pus and Removal of Membranes.**—A great deal of information is gained, as soon as the incision into the chest has been made, in reference to the expansibility of the lung. If this has not been much impaired, the pus will continue to escape with much force, especially during inspiration. Rapid evacuation is attended by some danger, from overdistention of the heart and vessels in the lung, and must be guarded against by interrupting the flow, from time to time, by inserting the index finger into the opening. If the lung expand promptly, its lower margin can often be seen through the opening toward the end of evacuation. The more the lung expands, the less the amount of air rushing through the opening into the chest. In order to prevent syncope upon the sudden diminution of intra-thoracic pressure, during evacuation of the pus, I have been in the habit of administering, before the anæsthetic is given, $\frac{1}{100}$ grain of atropia with ¼ grain of morphia, hypodermatically, with an alcoholic stimulant, by the stomach or rectum. In cases of empyema with a bronchial fistula, and in cases where respiration was so much embarrassed that I deemed the administration of an anæsthetic hazardous, I have repeatedly made the radical operation without narcosis, and the remedies which have just been mentioned answered an excellent purpose in diminishing the pain. If, as is so often the case, the pleura is lined with thick, partially-detached membranes, these should be removed with a dull curette, as they are invariably infected with pus-microbes, and their presence in the pleural cavity would prolong the infection and retard recovery.

(d) **Irrigation.**—Irrigation of the pleural cavity immediately after the operation is positively contra-indicated if a bronchial fistula is present, and it is superfluous if no putrefaction is present. In fetid empyema the cavity is washed out with warm, salicylated water until the fluid returns clear. This is followed by an irrigation, for a very short time, with a 1-to-1000 solution of corrosive sublimate. None of this solution should be allowed to remain in the pleural cavity.

(e) **Drainage.**—Rib resection should always be done in operations for empyema, as the space thus created offers ample room for the insertion of a large drain. I have frequently seen, after incision and drainage through intercostal space, circumscribed destructive processes of the margins of both ribs from pressure caused by the drainage-tube. Such pressure is not only a source of pain, but interferes also with free drainage. Resection of such a small portion of a rib does not add to the gravity of the operation, and is of the greatest utility in the subsequent management of the case. The best drain is a fenestrated rubber tube the size of the little finger, or two rubber tubes, somewhat smaller, stitched together. The tube should be from 4 to 6 inches in length, and always secured externally with a large safety-pin, to prevent its slipping into the pleural cavity. Non-observance of this little precaution has resulted in a great deal of trouble from drains becoming lost in the pleural cavity, The necessity of making a counter-opening and of establishing through drainage does not arise often, but, when such a procedure becomes necessary, it can readily be done with a large Péan forceps, which can be introduced into the anterior opening, and, by pushing it through the intercostal space behind, which has been selected for the counter-opening, an incision is made down upon its point, after which the opening is dilated and a long drain drawn through both openings. After completion of the operation a large antiseptic dressing is applied.

After-Treatment.—Daily change of the dressing and antiseptic irrigation will be necessary in fetid empyema, if the primary disinfection has not proved successful, in rendering the cavity free from putrefactive bacteria and necrosed material. In ordinary cases the dressing is not removed until it becomes saturated with the discharges, or if the temperature indicate the retention of septic material. Should, at any time, evidences of putrefaction or sepsis develop, antiseptic irrigations are positively indicated. A saturated solution of acetate of aluminum, an aqueous solution of tincture of iodine, a 2-per-cent. solution of boracic acid, or salicylated water can be used for this purpose; always using the solutions at blood-heat, as the irrigation of the pleural cavity with a cold or cool solution has in a number of cases resulted in death from shock. In one of my cases the wife of the patient irrigated the pleural cavity with what she afterward called a cool solution, and the patient died suddenly with symptoms of collapse. In another case, a patient 5 years of age, I made the irrigation myself, using only water, the temperature, as I afterward ascertained, being below blood-heat, when the patient suddenly became pulseless and the respirations ceased. Artificial respiration had to be continued for a considerable length of time, when, to my great relief, the child commenced to breath spontaneously and the pulse and color of the face returned. This experience warned me to exercise care in using solutions of a proper temperature in irrigations of the pleural cavity. The final expansion of the lung and obliteration of the pleural cavity are accomplished by the granulating process. The drain should be disinfected every time, and before it is re-inserted it should be dusted with iodoform.

(a) Multiple Resection of Ribs.—In cases of empyema where, after a radical operation, only partial expansion of the lung takes place, and the pleural cavity cannot close on account of the unyielding nature of the chest-wall, Estländer's operation of multiple resection of ribs is indicated. The operation consists in removing sections of 3 to 6 centimetres in length of all the ribs over the abscess-cavity, for the purpose of allowing the chest-wall to sink in, and thus remove the mechanical obstacle to closure of the pleural cavity. Through one incision over an intercostal space 2 adjacent ribs can be removed. If more than 2 ribs have to be resected, I prefer to make a single incision in the direction of the axillary line, through which, after dissecting back the superficial soft parts for 1 or 2 inches on each side of the incision, 6 or 8 ribs can be readily resected. Estländer's operation is absolutely valueless in cases where the lung is almost completely collapsed, as in such instances even the most extensive resection of ribs would fail in correcting the mechanical difficulty in the way of a definitive healing of the pleural abscess. The operation is also contra-indicated where further expansion of the lung depends on incurable lesions of this organ.

(b) Thoracoplastic Operation.—In obstinate cases of empyema, where even Estländer's operation fails in effecting a cure, and where the difficulties in the way are of a purely mechanical nature, Schede has recently described a procedure which, in reality, is a plastic operation. He not only makes resection of several ribs, but resects the entire thoracic wall over the cavity, with the exclusion of the skin. He makes a skin-flap with its base directed upward, corresponding in size to the cavity underneath, and then removes all of the ribs in the region to the same extent, and finally resects the remaining portion of the chest-wall. This operation exposes one side of the cavity completely, and the opposite wall is then covered with the skin-flap. The flap is not sutured, but kept in place by a compress of loose gauze corresponding in size and shape to the abscess-cavity. This operation deals more effectually with the mechanical difficulties resulting from imperfect expansion of the lung than Estländer's multiple resection of ribs, and will always be resorted to in proper cases where less heroic measures have failed in accomplishing the desired result.

LUNG-ABSCESS.

The successful treatment of abscess of the lung by operative procedure is one of the many achievements of modern surgery. Bull, of Norway, has collected 26 cases of abscess of the lung treated by incision and drainage, of which number 4 were cured, 6 improved, 9 relieved, and 7 were not benefited by the operation. Abscess of the lung is the result of a circumscribed suppurative inflammation of lung-tissue, or it develops after an attack of pneumonia or gangrene of the lung. If it follow pneumonia, a part of the solidified organ fails to undergo resolution and becomes the seat of secondary infection with pus-microbes. The abscess then forms by liquefaction of the inflammatory product, the same as in other tissues. Gangrene of the lung can only take place if the tissues become infected with putrefactive bacteria through the respiratory passages. If the gangrenous portion is limited in extent, and life is prolonged for a sufficient length of time, the dead tissue becomes detached, and is frequently eliminated in fragments through a bronchial fistula by coughing. The cavity which is formed in this manner suppurates, and is etiologically and clinically an abscess. A circumscribed suppurative pneumonia, resulting in the formation of an abscess, may occur around a foreign body which has lodged in one of the bronchial tubes. The clinical history of every abscess of the lung points to an antecedent suppurative pulmonary inflammation, with or without gangrene.

Diagnosis.—The surgeon diagnosticates the existence and location of an abscess in the lung by the same methods and means as when it is located in another organ. If, from the clinical history and physical examination of the chest, he has reason to suspect that the cavity is of a non-tubercular nature, he locates it as accurately as he can by the physical signs which are presented, and then demonstrates, *ad oculum*, the existence of a pus-cavity by exploring the lung with the needle of an exploring-syringe. Fenger was the first one in this country to locate an abscess of the lung by this means of examination, and to adopt treatment upon strict antiseptic surgical principles. Microscopical examination of the sputum is of great value in determining whether an abscess is tubercular or the result of a suppurative inflammation.

Methodical Exploration of Lung for Abscess.—If the physical symptoms point to a non-tubercular abscess in the lung, with or without a bronchial fistula, the surgeon will be able to determine the portion of lung involved by ascertaining over the abscess a limited area of dullness caused by condensation of lung-tissue around the abscess, and, if the abscess-cavity is filled by pus, by the presence of this fluid. If a bronchial fistula exist, auscultation will reveal the usual symptoms, caused by a cavity in the lung partially filled with blood. By means of percussion and auscultation it is ascertained when the abscess is nearest the surface, and at this point the lung is explored with a hollow needle, not exceeding in diameter an ordinary knitting-needle, and at least 4 inches in length, attached to an ordinary hypodermatic or exploring syringe. As a matter of course, the needle and surface must be rendered perfectly aseptic before the puncture is made. The needle is pushed through an intercostal space, corresponding to the location of the disease, in the direction of the centre of the inflammatory focus; its entrance into the abscess-cavity is attended by a sudden loss of resistance. Aspiration is now made, and if pus is found the diagnosis is made. If no pus is withdrawn the needle is pushed forward, and at different points aspiration is made. If pus is not found in one direction, the needle is partly withdrawn and pushed in another direction, and this and additional tracks are explored in the same manner until the cavity is located. An abscess-cavity only partially filled with pus may be entered at several points without finding pus. If the surgeon feel sure that the needle is in a cavity, it might be well to make aspiration with the patient in different positions, so as to bring the pus in contact with the needle; or, if this fail, to inject a mild antiseptic solution through the needle, which will be coughed up if the injection reach the cavity. *No operation on the lung must be undertaken for abscess until the exact location of the abscess has been demonstrated by exploratory puncture.*

Operation.—The first steps of an operation for abscess of the lung are the same as in radical operations for empyema. At least a section of one rib is removed. With few exceptions, the lung will have become adherent to the parietal pleura at the time the operation is undertaken, but if this is not the case it will become necessary to leave the operation unfinished rather than to risk an onset of suppurative pleuritis after the lung-abscess has been opened. In such a case, after the parietal pleura has been incised, the wound should be tamponed with iodoform gauze, and the opening of the abscess postponed until adhesions have formed. If adhesions make it safe to complete the operation, the abscess is again accurately located by exploring with a needle, and, while the needle is in the cavity, the lung is incised with the knife-point of Paquelin's cautery, using the needle for a guide. By making the incision with the actual cautery troublesome parenchymatous hæmorrhage is avoided, and at the same time the intervening lung-tissue is protected against infection by a tubular eschar; and last, but not least, such an opening is better adapted for subsequent free and effective drainage. A rubber drain, as large as the track made by the cautery, is inserted into the cavity. If the abscess communicate with the bronchial tubes irrigation cannot be practiced; if this is not the case the abscess is disinfected by irrigation with an antiseptic solution. In either case iodoformization of the abscess-cavity by dusting the drain with iodoform should always be done. If the first opening fail to drain the abscess satisfactorily, it may be necessary to make a counter-opening at the most dependent part of the cavity, and establish another and more efficient point for drainage (Vogt-Mosler).

The after-treatment in cases of lung-abscess treated by incision and drainage is the same as after radical operations for empyema.

SUPPURATIVE PERICARDITIS.

A suppurative inflammation of the internal surface of the pericardium results in an abscess of the pericardium, or *empyema pericardii*. The disease is characterized by evidences which indicate the presence of a suppurative inflammation and by physical signs which point to the presence of fluid in the pericardial sac. In some of the cases which have been reported it was attended by little general disturbance, no chill, and but little rise of temperature. If it occur as a complication of some other affections, the symptoms of the latter often obscure almost completely those of the former. In some of the cases the presence of pus was indicated by œdema in the præcordial region. If the quantity of pus is large, the pericardium is distended and the intercostal spaces in front of the effusion are more prominent than on the opposite side. The area of dullness, which can be mapped out accurately by percussion, corresponds with the size of the expanded pericardium. The impulse of the heart is felt less distinctly and is more diffuse than in a normal condition. A copious pericardial effusion always gives rise to orthopnœa.

Positive proof of the existence of a collection of pus in the pericardium can only be obtained by an exploratory puncture.

Puncture and Aspiration of Pericardium.—Puncture and aspiration of fluid from the pericardium is a comparatively harmless procedure, if it is practiced with ordinary skill and care.

West reports 79 cases of *paracentesis pericardii*. Of this number the operation was the cause of death in 1 case only, and in this instance the trocar which was used perforated the right ventricle. Six of the cases died during the first twenty-four hours, while in the remaining cases the immediate effect of the operation was beneficial, and a number of cases recovered permanently. In puncture of the pericardium for diagnostic or therapeutic purposes, the trocar should always give way to a medium-sized needle of an exploring-syringe or aspirator. The puncture is made under strict antiseptic precautions. The structures to be avoided are the internal mammary artery, the pleural cavity, and the heart. The safest place for puncture is, in ordinary cases, the fifth left intercostal space, about half an inch or an inch from the margin of the sternum, through which the needle should be pushed in a slightly upward and outward direction, so as to avoid wounding the heart. It has to travel $1\frac{3}{4}$ to 2 inches before it enters the pericardial cavity. If pus is found the case must be treated by

Incision and Drainage of the Pericardium.—Instead of using a trocar, it is much better to make an incision in the fifth intercostal space, using the needle with which the exploratory puncture was made as a guide. The same precautions to prevent syncope as were recommended in the radical operation for empyema should be resorted to in these cases, and chloroform is preferable to ether as an anæsthetic. The intercostal incision need not exceed an inch in length, and, as soon as the pericardium has been opened sufficiently to allow the escape of pus, a dressing forceps may be inserted, and the opening enlarged sufficiently to enable the introduction of a drainage-tube the size of an ordinary lead-pencil.

Irrigation of the pericardial cavity is to be avoided unless suppuration is complicated by putrefaction. The drainage-tube should not project sufficiently into the pericardial sac to come in contact with the heart, and should always be of soft material, so as not to injure the heart should it be too long. The antiseptic dressing can be retained most effectually with several strips of rubber adhesive plaster, which should be long enough to encircle the whole chest. Gussenbauer, in a patient 15 years of age, suffering from suppurative pericarditis after osteomyelitis, resected part of the fifth rib near the sternum before incising the pericardium, and the patient recovered. This modification of the ordinary operation by incision through the fifth intercostal space will occasionally present decided advantages in the surgical treatment of pericardial empyema.

SUPPURATIVE PERITONITIS.

A great deal of confusion has recently arisen in the use of the terms *septic* and *suppurative* peritonitis. Etiologically, they are identical; clinically, they differ in so far that septic peritonitis is generally diffuse, and leads to a rapidly fatal termination; while what is known as suppurative peritonitis is more frequently circumscribed, and more amenable to surgical treatment. Both forms are caused by infection with pus-microbes. In the septic variety death results from sepsis before the pus-microbes have had time to produce their specific pathogenic effect on the histological elements which are destined to become converted into pus-corpuscles. In suppurative peritonitis the pus-microbes are either less in number or they meet with conditions less favorable to the production of a fatal amount of ptomaines, or, finally, the peritoneum is in a condition which is unfavorable to the entrance of pus-microbes or their ptomaines into the circulation.

Bacteriological and Experimental Researches.—A number of original investigators have studied the etiology of peritonitis experimentally, and their work has been of great practical value in showing that suppurative peritonitis is not only caused by the action of pus-microbes, but that it is equally essential that certain conditions must be present in the peritoneal cavity which enable the pus-microbes to produce their specific pathogenic effects. Pawlowsky made ten series of experiments on 101 animals. The chemical irritants, or cultures, were introduced into the peritoneal cavity through the canula of a small trocar under strict antiseptic precautions, and the small wound was carefully sealed with iodoform collodion. The first series consisted of experiments with croton-oil on 3 dogs and 9 rabbits. The amount of croton-oil injected in each case varied from 6 drops to $\frac{1}{10}$ drop. The smallest doses produced no effects. Large doses produced a severe, acute, hæmorrhagic peritonitis, the intensity of which was proportionate to the quantity of the irritant injected. The peritoneal exudation, under the microscope, was seen to contain red and white blood-corpuscles. Inoculations of different nutrient media with the fluid yielded negative results. In the next series of experiments, an aqueous solution of trypsin and pancreatin was injected for the purpose of determining whether the digestive ferments, in the event of intestinal perforation, could produce peritonitis. The experiments established the fact that trypsin acts as a powerful irritant upon the peritoneum. Injection of $\frac{1}{2}$ gramme of trypsin, dissolved in distilled water, caused in rabbits a severe hæmorrhagic peritonitis, with a copious exudation, and death in from four to four and a half hours. In doses of $\frac{1}{4}$ to $\frac{1}{10}$ gramme the same local condition was produced, but death did not occur until twenty to twenty-four hours after the injection. One-hundredth (.01) of a gramme produced no symptoms. Nutrient media inoculated with the products of inflammation remained sterile. Next, the peritoneal cavity was infected with plate cultures of different microbes suspended in sterilized water. The first experiments were made with non-pathogenic microbes. Four rabbits and one dog were injected with large quantities of a micrococcus, which was obtained from a plate culture inoculated with pus; the micrococcus was exactly similar to the staphylococcus pyogenes albus, for which it was first mistaken. Later, it was shown that it was not a pus-microbe, as it did not liquefy gelatin. All of the animals recovered. Two rabbits inoculated with an entire culture of yellow sarcinæ upon agar-agar, mixed with $\frac{1}{10}$ drop of croton-oil, also recovered. The experiments with pathogenic microbes always produced positive results. Three series, with three separate micro-organisms, were made next. The staphylococcus pyogenes aureus, grown from osteomyelitic pus, was first used. In 17 out of 41 experiments this microbe alone was used; in 11 it was mixed with croton-oil, in 6 with trypsin, and in 7 with agar-agar. In all cases where pure cultures were used peritonitis was produced, the type varying according to the number of microbes used. The same microbes could be cultivated upon proper nutrient media from the different inflammatory products. In hardened specimens of the inflamed peritoneum, stained with different coloring agents, the micro-organisms could be seen in the lymph-spaces. The suppurative type of peritonitis thus artificially produced became more apparent the longer life was prolonged. An entire agar-agar culture of the bacillus pyocyaneus caused death from septic peritonitis in from twenty-four to forty-eight hours. One-fifth of this quantity proved harmless. The next series of experiments was made to ascertain the cause of peritonitis after intestinal perforation. The fresh intestinal contents of a healthy animal, just killed, were divided into three parts, one of which was at once injected into several rabbits, without filtration, in doses of 1 syringeful. The second portion was filtered, and of the filtrate from 2 to 3 syringefuls were injected into each rabbit. The third portion was sterilized, according to Tyndall's directions, for eight days, and then 1 syringeful was injected into the abdominal cavity of each animal. The results were as follow: Four rabbits died of fibrinous, suppurative peritonitis from the injections with the first portion. Four rabbits injected with the filtered fæces recovered, as did one animal inoculated with the sterilized portion.

At the necropsy particles of the fæces were found in the peritoneal cavity covered with fibrin, and a peculiar, short bacillus was found in the inflammatory exudate. This bacillus he believed to be the cause of peritonitis, and consequently termed it *bacillus peritonitidus ex-intestinalis cuniculi.* The cultures of this bacillus upon agar-agar he describes as shining, grayish-white, oil-paint-like colonies. With cultures of this bacillus he made 9 experiments on rabbits and 2 on dogs. Every animal which received an entire agar-agar culture died of hæmorrhagic peritonitis in from twenty to twenty-four hours. In smaller quantities, death from the same cause sometimes did not occur until at the end of the third day. Still smaller doses produced a suppurative peritonitis and death after a number of days. Of the 2 dogs, each injected with an agar-agar culture, 1 died after twenty-four hours of septic peritonitis, the other recovered after an illness of several days' duration. In the fatal cases the bacillus was found in different organs, and could again be reproduced by inoculations with infected tissues upon nutrient media. This author maintains that the fibrinous form of peritonitis is the least dangerous, as the layers of fibrin tend to limit the entrance of microbes into the circulation, while they also retard the local diffusion of the injection. The fibrino-suppurative variety is the next least dangerous form, while in the most rapidly fatal cases of septic peritonitis the local lesion is not characterized by any macroscopical tissue changes. Wegner has shown by his experiments that a great variety of fluids from septic microbes, such as water, bile, urine, blood, etc., can be injected into the peritoneal cavity of rabbits without any serious results following; even large quantities of unfiltered air, when introduced in the same manner, proved innocuous. Putrescible substances, when injected in small quantities, were rapidly absorbed without producing peritonitis; but when the quantity injected was large, and insufflation of unfiltered air was practiced at the same time, peritonitis, with putrefaction and death from septic intoxication, occurred. Grawitz proved that saprophytic bacteria, when injected into a normal peritoneal cavity, were promptly destroyed and absorbed. In cases in which the injection was made into a peritoneal cavity which had previously undergone alterations by injury or disease, or in which the quantity of fluid was too great for speedy absorption, symptoms of intoxication, as described by Weber, resulted, but these symptoms were unaccompanied by suppurative peritonitis. A healthy peritoneal cavity has also been found capable of disposing of a limited quantity of pure cultivations of pus-microbes, the microbes being removed by absorption and destroyed in the circulation, or eliminated through the excretory organs. But when pyogenic organisms are introduced into an abdominal cavity, in which the absorptive capacity of the peritoneum has been diminished or suspended by antecedent pathological conditions, suppurative peritonitis is the usual result. When pus-microbes are introduced in large quantities, even into a healthy peritoneal cavity, the preformed ptomaines, by their chemical action, so alter the tissues that the process of absorption is impaired, and suppurative peritonitis again results in consequence of the retention of pus-microbes in tissues prepared for their pathogenic action.

Orth agrees with Grawitz, that when a pure culture is injected into a healthy peritoneal cavity suppuration does not necessarily take place. But his experiments prove, what is of the greatest practical interest, that, if the peritoneum is wounded under antiseptic precautions, peritonitis invariably follows, if suppuration exist elsewhere in the body at the same time. If, for instance, an abscess in the subcutaneous tissue was artificially produced in animals, and then the intestine was rendered temporarily impermeable, death from suppurative peritonitis was the rule. The same result followed if the pus-microbes were injected directly into the circulation, but not if they were introduced through the alimentary canal. Rinne is of the opinion that, on account of the rapidity with which absorption takes place in the peritoneal cavity, the peritoneum, when in a normal condition, is almost immune to infection with pus-microbes. He injected from 30 to 35 cubic centimetres of a pure culture of pus-microbes, suspended in sterilized water, into the peritoneal cavity of healthy animals, and never succeeded in this manner in producing peritonitis. He had no better success with injections of a mixture of a gelatin culture of staphylococcus pyogenes aureus and a turbid bouillon culture of the same coccus. He also made daily injections with a putrid fluid, to which was added a culture of the staphylococcus pyogenes aureus, without producing peritonitis. The experiments, as a rule, were made on dogs, although, in several instances, rabbits, guinea-pigs, and white rats were used. He believes that the difference in the results obtained by him and Grawitz, as compared with Pawlowsky, consists in the nature of the abdominal wound. Pawlowsky made an incision down to the muscles and then perforated the abdominal wall with a blunt trocar; while he and Grawitz used a sharp, hollow needle for making the intra-peritoneal injection. To prove that his injections reached the peritoneal cavity, he added coal-dust to the fluid, which he found at the post-mortems as fine particles clinging to the peritoneal surface.

Clinical and Bacteriological Studies.—Fränkel found the streptococcus pyogenes in a great variety of puerperal diseases, especially in cases in which the local affection implicated the lymphatic vessels. In such cases the microbes found entrance into the pelvic tissues from abrasions or ulcers in the vagina, and by extension of the inflammatory process the broad ligaments and the peritoneum are successively reached;

after the peritoneum has once been reached rapid diffusion takes place, and, finally, the diaphragm and pleura are implicated in the same process, and the microbes reach the blood and cause sepsis and pyæmia.

Weichselbaum has shown that peritonitis is not always caused by pus-microbes, as has been heretofore believed, as he found the diplococcus of pneumonia unaccompanied by any other micro-organism in 3 cases of peritonitis. In 1 case peritonitis and pneumonia existed at the same time; in the other double pleuritis followed the peritonitis; but in the last case peritonitis was undoubtedly primary, and, in the absence of any other microbes in the products of the inflammation, must have been caused by the diplococcus of Friedländer. There can be no doubt that septic peritonitis may be caused by pathogenic microbes which, at present at least, are not classified with the pus-microbes; but suppurative peritonitis can have no other bacteriological cause, and in most cases of septic peritonitis infection with pus-microbes can be demonstrated by clinical evidences as well as bacteriological and experimental demonstration.

Difference between Plastic and Suppurative Peritonitis.—The greatest clinical difference between simple or plastic peritonitis produced by trauma or chemical irritants and septic or suppurative peritonitis consists in the cause and extent of the inflammation. Plastic inflammation produced by aseptic causes remains limited to the seat of trauma or chemical irritation, and does not extend much beyond the surface-area to which the stimulus is applied; while septic peritonitis is always characterized by its progressive character, as the cause upon which it depends is reproduced within the peritoneal cavity. A plastic peritonitis is attended by febrile disturbances, caused by the introduction into the circulation of the products of coagulation necrosis or metabolic tissue changes; in septic peritonitis the general symptoms are produced by the entrance of pus-microbes into the general circulation and their ptomaines, both of which are also reproduced in the blood and other organs of the body in which secondary localization may take place.

The Causes of Suppurative Peritonitis.—Experimental research has demonstrated that in the causation of suppurative peritonitis two conditions must be present at the same time: 1. Pyogenic bacteria. 2. A wound of the peritoneal surface, or antecedent pathological conditions which diminish the absorptive capacity of the peritoneum. The microbic cause is the essential etiological factor, as without it the other conditions would not result in this form of peritonitis. If pus-microbes are introduced into the peritoneal cavity in sufficient quantity, suppurative peritonitis is produced, as the preformed ptomaines create the indirect etiological conditions. A number of bacteria which at present are not classified with the pus-microbes may, under certain favorable conditions, manifest pyogenic properties; and thus, when introduced into a peritoneal cavity predisposed to suppuration, cause an attack of suppurative peritonitis. Thus we have seen that Weichselbaum has found the diplococcus of pneumonia in the inflammatory product of 3 cases of peritonitis, and as no other microbes were present it is reasonable to assume that suppuration was caused by this microbe. In serous cavities gonorrhœal pus produces, as a rule, a circumscribed abscess. Sinclair, in his excellent monograph on "Gonorrhœal Infection in Women," after describing the gonorrhœal infection from the vagina, says: "The proper character and the results of the pathogenous activity of the gonorrhœic microbes are therefore seen—pure and unadulterated in the tube. They cause purulent inflammation of the mucous membrane, but the surrounding connective tissue remains free from them. The gonorrhœic tubal pus is evacuated into the peritoneum, and, whereas in other conditions the bursting of an abscess into the abdominal cavity is followed by the gravest consequences, in this case the whole process terminates with a circumscribed inflammation, encapsuling the exuded pus. The cause of this difference is the varying pathogenic value of the organisms which are contained in the pus. A puerperal pelvic cellulitic abscess, bursting into the peritoneum, causes general peritonitis, because it contains pyogenous streptococci, which rapidly multiply in serous cavities, and are capable of exerting the most deleterious effects. Gonorrhœal tubal pus cannot do this; its microbes do not find in the peritoneum conditions for their increase; the pus, therefore, acts as an aseptic foreign body, becomes encapsuled, and is finally absorbed. Practically, it is well known that when gonorrhœal infection extends from the Fallopian tubes to the peritoneum by leakage of pus into the peritoneal cavity from the peritoneal extremity of the tube, or rupture of a pus-tube, the result is a circumscribed suppurative peritonitis, with the formation of a circumscribed abscess."

That this favorable termination does not invariably follow gonorrhœal infection of the peritoneal cavity is well shown by a case reported by Lovén, which is by no means an isolated one. The source of infection could not be learned in this case, but the diagnosis of gonorrhœic ascending infection was positive. The disease commenced as an ordinary vulvo-vaginal blennorrhœa, which consecutively extended to the uterus, Fallopian tubes, and terminated in pelvic and diffuse peritonitis. It is possible that in this particular case a secondary infection with pus-microbes had taken place, as, at the necropsy, chain cocci were found in the peritoneal cavity. The relation of the streptococcus of erysipelas to peritonitis will be considered in the chapter on Erysipelas. Abdominal surgeons are very well aware of the clinical fact that septic or suppurative peritonitis, after laparotomy, is more prone to develop if fluids, and especially blood, are allowed to remain in the abdominal cavity; and consequently resort to a careful toilet of the cavity, and, if there is any reason to expect a re-accumulation, to drainage. Fluid in the peritoneal cavity prevents the removal of the pus-microbes by absorption, and if they remain they multiply and cause peritonitis. For years it has been customary to resort to the use of opium in the prevention and treatment of peritonitis, until Tait showed the fallacy of such treatment and recommended cathartics in threatened cases of peritonitis. The treatment of incipient peritonitis by a brisk saline cathartic is now generally practiced, and the results have been exceedingly satisfactory. What is the *modus operandi* of saline cathartics in the prevention of diffuse septic peritonitis? The most rational answer to this question is that a brisk saline cathartic promotes absorption of fluids from the peritoneal cavity, and by so doing removes the indirect causes of peritonitis, and, at the same time, favors the elimination of pyogenic microbes. Intra-abdominal wounds not covered with peritoneum are potent factors in the development of peritonitis in an abdominal cavity which is not absolutely aseptic, as the raw surfaces furnish a considerable quantity of wound-secretion, on the one hand, and, on the other, diminish the absorptive capacity of the peritoneum. This cause of peritonitis should be avoided as far as possible, in all intra-abdominal operations, by avoiding unnecessary injury to the peritoneum, and by covering denuded surfaces with this membrane wherever it can be done. Another indirect cause of peritonitis is intestinal obstruction. The intestine above the seat of obstruction becomes dilated, congested, softened, and, in consequence of these changes, permeable to pathogenic microbes, which are always present in the intestinal canal under these circumstances.

Alapy has made a series of experiments in Weichselbaum's laboratory to ascertain if pathogenic microbes could pass through the healthy stomach into the intestines. He experimented with pus-microbes and the streptococcus of erysipelas. From these experiments he came to the conclusion that the virulence of these microbes is destroyed in a healthy stomach, but when the gastric secretion has suffered diminution of acidity, or has become alkaline, the microbes do not lose their pathogenic properties, and pass into the intestines in an active condition. In cases of intestinal obstruction the physiological functions of the stomach are disturbed, and conditions are created which preserve the virulence of pathogenic micro-organisms on their way into the intestinal canal. The immediate cause of death in many cases of intestinal obstruction is diffuse septic peritonitis. In the different forms of perforative peritonitis the disease is caused by the escape of fluids containing pyogenic bacteria, and the type and gravity of the disease is greatly modified by the amount of fluid which enters the peritoneal cavity and the number of microbes which it contains. Perforation of a typhoid or tubercular ulcer is always a grave occurrence, as the fluid which escapes is usually considerable in quantity and contains numerous pathogenic microbes. Perforating ulcer of the stomach is more frequently followed by circumscribed plastic peritonitis, which shuts out the general peritoneal cavity. Perforation of the appendix vermiformis is followed as often by circumscribed suppurative peritonitis as by diffuse septic peritonitis. The same can be said of perforation of the gall-bladder.

Symptoms and Diagnosis.—Diffuse septic peritonitis spreads over the entire peritoneal cavity almost with lightning speed. The first symptoms are those of shock. If the disease follow an abdominal section, it is often difficult to determine whether the conditions presented are due to shock or diffuse peritonitis, as the latter may set in in a few hours after the operation and prove fatal within twenty-four hours. The temperature is variable. It may remain normal or become even subnormal, or it may at first be only slightly increased and gradually reach 102° to 104° F. Vomiting and diarrhœa are frequently conspicuous symptoms. In other cases the symptoms point to intestinal obstruction. In extensive plastic peritonitis the immobilization of a considerable portion of the small intestine may give rise to persistent vomiting and absolute constipation. Again, arrest of the fæcal circulation may be caused by the tympanites alone, while perforative peritonitis is attended by a local and general shock, which causes intestinal paresis through the sympathetic nerves. Heusner has observed that perforative peritonitis gives rise to disturbances simulating intestinal obstruction by arresting intestinal movements. He narrates the histories of 2 cases of this kind in which the symptoms of intestinal obstruction were so prominent that laparotomy was performed. In both cases perforative peritonitis, but not occlusion, was found. Henrot, in his classical monograph on "Pseudo-Strangulation," describes a number of cases of perforation of the gall-bladder and the processus vermiformis, where the symptoms during life had pointed so strongly to the existence of intestinal obstruction that a wrong diagnosis was made by able clinicians. He also calls attention to those cases of paralytic obstruction which are often observed after herniotomy, and in cases of strangulation of the appendix vermiformis and testicle. The intestinal paresis, where it is not the result of inflammation, must be looked upon as a reflex symptom.

Physical signs and symptoms are sometimes utterly inadequate to distinguish between acute intestinal obstruction and diffuse peritonitis.

In differentiating between these two conditions, it must be remembered that, in the absence of a tumor, absolute constipation and fæcal vomiting are the most characteristic symptoms of obstruction, and that in peritonitis the pain is severe and continuous, with diffuse tenderness, tympanites, and absence of visible intestinal coils. In mechanical obstruction of the bowels the temperature is, as a rule, not above normal unless complications have set in; while in peritonitis a rise in temperature is the rule, although in some of the gravest cases it is subnormal. Many cases of supposed recovery from intestinal obstruction without operation undoubtedly were cases of dynamic obstruction, and the recovery was either entirely spontaneous or facilitated by means which assisted in the restoration of peristaltic action. In 1851 a patient was admitted into Dupuytren's ward with well-marked symptoms of acute intestinal obstruction. This eminent surgeon gave it as his opinion that without an operation a fatal termination was inevitable, but the patient objected to the operation and was transferred to another ward, where he recovered in three days under the use of simple cathartics.

Numerous similar cases could be cited in illustration of the difficulty of differentiating in all cases between mechanical occlusion and dynamic obstruction. In cases of perforative peritonitis and peritonitis with putrefaction the presence of gas in the free peritoneal cavity gives rise to an important physical sign. In tympanites from peritonitis and intestinal obstruction, the distended intestines push the liver in an upward direction; hence, on percussion, the liver dullness is transferred higher up. But, under the circumstances mentioned above, the gas in the free abdominal cavity occupies the space between the liver and the chest-wall; consequently, the liver dullness has disappeared, and the space over the organ is tympanitic on percussion. One of the most constant signs in peritonitis is the small, rapid, compressible pulse. In diffuse peritonitis it usually ranges between 120 and 140. In rapidly fatal diffuse septic peritonitis pain is often wanting. In circumscribed peritonitis pain and tenderness are limited to the affected region. Tympanites is often a most distressing symptom in circumscribed peritonitis, and may be entirely absent in the most fatal form of septic peritonitis. Rigidity of the abdominal muscles is an indication of peritonitis, while it is absent in uncomplicated intestinal obstruction. In suppurative peritonitis the presence of pus is indicated by the physical symptoms arising from the accumulation of fluid, either in the free peritoneal cavity or in a circumscribed space of it. If the pus is not confined by adherent intestines and plastic exudation, it will gravitate toward the most dependent portion of the peritoneal cavity, and on this account the area of dullness will vary according to the position of the patient. In circumscribed suppurative peritonitis the pus is confined in a limited space by adherent abdominal organs and fibrinous exudation, and will then present all the signs and symptoms of a deep-seated abscess. To determine the character of peritoneal effusion, or of the contents of a circumscribed intra-peritoneal inflammatory swelling, it is necessary to resort to an exploratory puncture. The needle is inserted at a point where the fluid is in contact with the abdominal wall, and, in the circumscribed form of peritonitis, in a place where the puncture can be made without traversing the free peritoneal cavity.

Treatment.—In perforative peritonitis cathartics are absolutely contra-indicated, as increased peristalsis would aggravate the existing conditions by increasing the extravasation and by preventing limitation of the infection. In such cases opium should be administered to diminish the peristalsis, to relieve pain, and to diminish shock. The subsequent safety of the patient will rest on an early radical treatment by laparotomy. Unless the location of the perforation can be ascertained beforehand, the incision should be made in the median line. In cases of perforation of the appendix vermiformis, an incision extending from the middle of Poupart's ligament to a point half-way between the anterior-superior spinous process of the ilium and umbilicus will secure most direct access to the seat of perforation. Perforating tubercular and typhoid ulcers are found most frequently in the ileo-cæcal region. If, on opening the abdominal cavity, the perforation cannot be readily found, it is better to resort to rectal insufflation of hydrogen-gas at once, which will show with unfailing certainty not only that a perforation exists, but also its exact location. In multiple perforations the same diagnostic test is almost indispensable, as it will avoid the great mistake of leaving a perforation unsutured. The perforations are treated in the same manner as an incised wound. Care must be taken to suture the opening in a direction that will interfere the least with the lumen of the intestine. Fine aseptic silk should always be used in preference to catgut; at least two rows of sutures must be applied.

After suturing the perforation the abdominal cavity is washed out freely with sterilized water. Drainage in these cases must never be omitted, as the operator has no assurance that the peritoneal cavity has been rendered perfectly aseptic. A threatened septic peritonitis after laparotomy can often be aborted by giving half an ounce of sulphate of magnesia, dissolved in a glassful of water, upon the appearance of the first symptoms. The action of the saline cathartic can be hastened and its beneficial effects increased by the administration of a turpentine enema. After the bowels have been moved thoroughly opium can be given in sufficient doses to relieve pain. If the symptoms do not subside under this treatment, the abdominal wound is opened sufficiently to permit free irrigation with salicylated water, and a Keith drain is inserted. The free end of the drainage-tube is kept plugged with aseptic cotton. The fluid in the tube is removed every two or three hours by aspiration. Many surgeons of the present time doubt the occurrence of peritonitis without a local source of infection, and there can be no doubt that so-called spontaneous peritonitis without such a local focus is exceedingly rare, but its existence cannot be denied. If suppuration in a joint in the pleural cavity in the pericardium can occur without such a direct local cause, there is no reason why suppurative peritonitis should not, at least in exceptional cases, have a similar origin. A *locus minoris resistentiæ* of a non-suppurative type in any part of the peritoneal cavity can determine localization of pus-microbes here as well as in any other part of the body. In opening the abdomen for the evacuation of pus, the surgeon must look for a primary lesion, but he will not always find it, as it is not invariably present. Diffuse septic and suppurative peritonitis are seldom, if ever, cured by laparotomy. Localized suppurative peritonitis brought about by curable causes is amenable to successful surgical treatment. An operation is indicated as soon as the presence of pus is ascertained. Delay is dangerous in these cases, as the delicate walls, composed of plastic exudation, may yield to the pressure and extravasation of pus, infect a new portion of the peritoneal cavity, or perhaps its entire extent. In circumscribed suppurative peritonitis the incision is to be made at a point where the pus is in contact with the abdominal wall. The abdomen is to be opened by a careful dissection, and if the incision lead directly into the pus-cavity this is drained and washed out with sterilized water or a weak antiseptic solution. If, on cutting through the peritoneum, no pus is found, and the peritoneal cavity has been opened, it is not safe to evacuate the pus until the peritoneal cavity has been shut out by suturing the abscess-wall to the parietal peritoneum, or packing the wound for a few days with iodoform gauze, and postponing the opening of the abscess until firm adhesions have formed between the margins of the wound and the surface of the abscess-wall. This method of operating must be frequently resorted to in the treatment of pelvic abscess, abscess of the liver, and empyema of the gall-bladder. If the primary disease which has caused the intra-peritoneal suppuration can be discovered, this must receive special attention. In circumscribed suppurative peritonitis in the right iliac region caused by perforation of the appendix vermiformis, the appendix must be looked for, and when found perforated it is excised near its attachment to the cæcum after tying its base with a fine silk ligature; or, if this cannot be done, it may be slit open and drained, as was done successfully by Tait.

All operations for suppurative peritonitis are to be conducted upon rigid antiseptic principles, and the treatment is to be followed without relaxation during the entire after-treatment. As patients suffering from peritonitis are always greatly debilitated from the effects of the disease as well as from lack of solid food, which for well-founded reasons must be withheld, every effort should be made to sustain strength by the systematic administration of liquid nourishment and alcoholic stimulants. Absolute rest must be enforced for the purpose of limiting the extension of the disease and with a view of aiding the process of repair.

CHAPTER XII.

SEPTICÆMIA.

SEPTICÆMIA, septæmia, sepsis, are synonymous terms used to designate a general febrile affection caused by the introduction into the circulation of the products of fermentation or putrefaction, and which is characterized by definite blood-changes, a typical series of inflammatory processes, a peculiar group of nervous symptoms and critical discharges. Clinically, and probably etiologically, it is closely related to pyæmia. The older pathologists entertained the belief that in cases of septicæmia the blood itself was the seat of putrefactive changes. At present it is generally conceded that it results from the introduction into the circulation of septic micro-organisms or their ptomaines. The symptoms do not suffice for a full characterization of the disease, but the specific infection is the integral and essential factor.

BACTERIOLOGICAL RESEARCHES.

Septic processes were among the first to excite interest in the part played by micro-organisms in disease. Although some of the best pathologists have been diligently investigating this subject for years, we still remain in the dark concerning its true etiology and its relation to other infective processes. True sepsis is now regarded as a general infection from some local source, unattended by any gross pathological changes. Some writers have claimed the etiological difference between septicæmia and pyæmia to be a quantitative and not a qualitative one, while others maintain that pyæmia is a specific disease *sui generis*, and that it is in no wise related to sepsis. There can be no doubt that true progressive sepsis, if not invariably, is, at least frequently, caused by the same microbes which produce pyæmia. As we have seen in the foregoing chapter, the same microbes, when introduced into the peritoneal cavity, may either cause a circumscribed suppurative peritonitis or a diffuse septic peritonitis, with all the clinical features of progressive sepsis. The first reliable investigations into the microbic origin of sepsis were made by Rindfleisch in 1866, and, somewhat later, by Klebs, Recklinghausen, Waldeyer, and Hueter. Rindfleisch found bacteria in abscesses, while the researches of Klebs initiated a new era in the etiology of septic diseases. Klebs differentiated between septicæmia and pyæmia.

although he claimed that putrid intoxication and septic infection were the same. In the tissues altered by septic processes, and in the lymph-spaces and in the blood, he found a microbe, a round coccus, isolated and in groups, which he termed *mikrosporon septicum*.

Septicæmia in Mice.—One of the best descriptions of true progressive septicæmia that has ever been given is by Koch on septicæmia in mice. He used the same method which was followed by Coze, Feltz, and Davaine. He injected putrid fluids, decomposed blood, putrefying blood, under the skin in mice. He found that the virulence of these fluids was attenuated by age. Blood that had putrefied only for a few days, in 5-drop doses, killed a mouse within a short time. In this case marked symptoms were observed in the animal immediately after the injection.

The animal became very restless, running about constantly, but showing great muscular prostration and uncertainty in all its movements; it refused food, the respiration became irregular and slow, and death took place within eight hours. The greater portion of the fluid injected was found after death not to have been absorbed. No inflammation at the seat of injection. No macroscopical pathological changes were found in any of the internal organs. Blood taken from the right auricle and injected into another mouse produced no symptoms. No bacteria could be found in the blood or any of the internal organs. Koch concluded that death was not caused by bacteria, but by the introduction into the circulation of a preformed poison contained in the putrid fluid, as when smaller doses were used the symptoms of intoxication were less marked, and when the quantity was reduced to 1 drop the animal often recovered without manifesting any morbid symptoms. About one-third of the animals which had received 1 or 2 drops of the fluid subcutaneously remained well for about twenty-four hours, when an increased secretion from the conjunctiva was observed; at the same time the animal showed signs of great muscular weakness. It then ceased to take food; its respirations became slower, prostration became more and more marked, and death came on almost imperceptibly. After death the animal remained in the sitting posture with its back strongly bent. Death occurred in from forty to sixty hours after inoculation. The only post-mortem change noticed was a slight subcutaneous œdema at the point of injection, and this was not constantly present.

Koch then experimented with the œdema-fluid and blood of mice that had died of sepsis, $\frac{1}{10}$ drop of which was injected into another mouse, when exactly the same symptoms and result were produced in the latter animal, after the same lapse of time and in the same order as in the former.

From this second animal a third was infected in like manner with identical results Successive inoculations proved that the virus could be propagated indefinitely from animal to animal without losing its virulence. He could communicate the disease with certainty by passing the point of a scalpel, which had been in contact with the infected blood, over a small wound of the skin. The blood of the animals which became

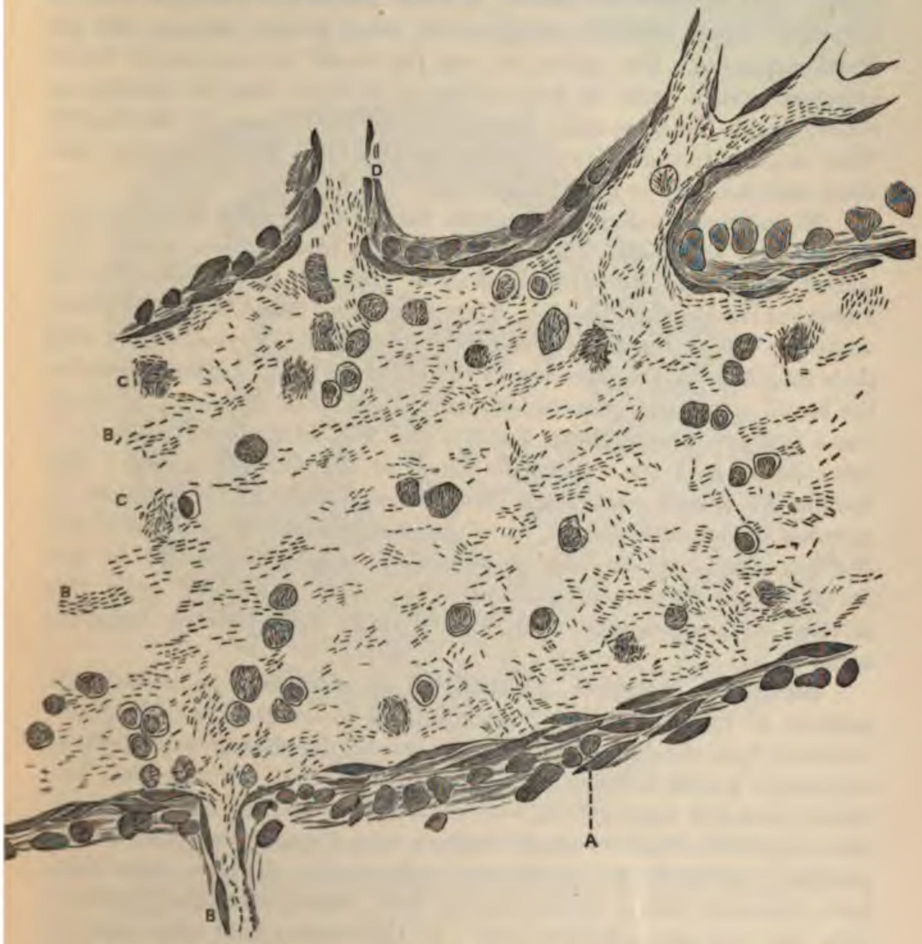

FIG. 66.—VEIN OF THE DIAPHRAGM OF A SEPTICÆMIC MOUSE. × 700. (*Koch.*)*

A, nuclei of the vascular wall; B, septicæmic bacilli; C. white blood-corpuscles which have become transformed into masses of bacilli; D, capillaries opening into vein.

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* Figs. 66, 67, and 68 are copied from "Traumatic Infective Diseases," by permission of the New Sydenham Society, London.

ill after injection of 1 to 10 drops of putrefying blood was found to contain, as a rule, different varieties of bacteria in small numbers, micrococci, and large and small bacilli. If, however, it died after inoculation with putrefying or septicæmic blood, small bacilli alone appeared in the blood. This result was constant, and the bacilli were always in large numbers. These bacilli lie singly or in small groups between the red blood-corpuscles. One often can see the bacilli in septicæmic blood attached to each other in pairs, either in straight lines or forming an obtuse angle. In some cases Koch has also seen spores in the bacilli. Their relation to the white corpuscles is peculiar. They penetrate into these, and multiply in their interior.

Microscopical examination of the tissues at the point of inoculation showed that the bacilli entered the capillary blood-vessels, where they caused such extensive alterations as to give rise to extravasation of numerous red blood-corpuscles. They were never found in the lymphatic vessels. Within the blood-vessels they are almost always arranged with their long axis in the direction of the blood-current. In the capillaries the bacilli congregate, particularly at the points of division, but never cause complete obstruction. Rabbits and field-mice proved immune to inoculations with the septicæmic blood of the domestic mouse. The bacillus of Koch's septicæmia can be cultivated upon a mixture of aqueous humor and gelatin, or of gelatin, peptone (1 per cent.), salt (0.6 per cent.), and sodium phosphate in sufficient quantity to render the mass alkaline in reaction. The bacilli grow well upon this mixture, and by repeated and rapid division form peculiar branched series.

Septicæmia in Rabbits.—Although Koch was unable to produce septicæmia in rabbits, either by injections or inoculations of septicæmic products from the domestic mouse, he caused the disease artificially by injecting a putrid infusion of meat. In these cases the injection produced extensive suppuration, with putrefaction, and the animals died in three days and a half. Various bacteria were found in the inflammatory product. At the border of the local inflammation the connective tissue was infiltrated with a turbid, serous fluid, which contrasted strongly with the brownish offensive pus. In this œdema-fluid only cocci of an oval form were found. In the blood similar microbes were found, though only in small numbers. Some of the small veins in the spleen and kidneys were seen to be completely blocked with the same microbe.

Two drops of the œdema-fluid were injected under the skin of the back of a second rabbit. The animal died in twenty-two hours, and here, in the vicinity of the injection, not a trace of suppuration could be found. Hæmorrhagic extravasations were found in the inflamed œdematous connective tissue. No alterations were found in the heart and lungs. In this animal the oval micrococci were alone present in the œdema-fluid. Micrococci were also found in the capillary vessels in different organs; in some of them the lumen of the vessels was completely blocked. In the capillary vessels surrounding the intestinal glands numerous obstructing masses of the bacilli were present.

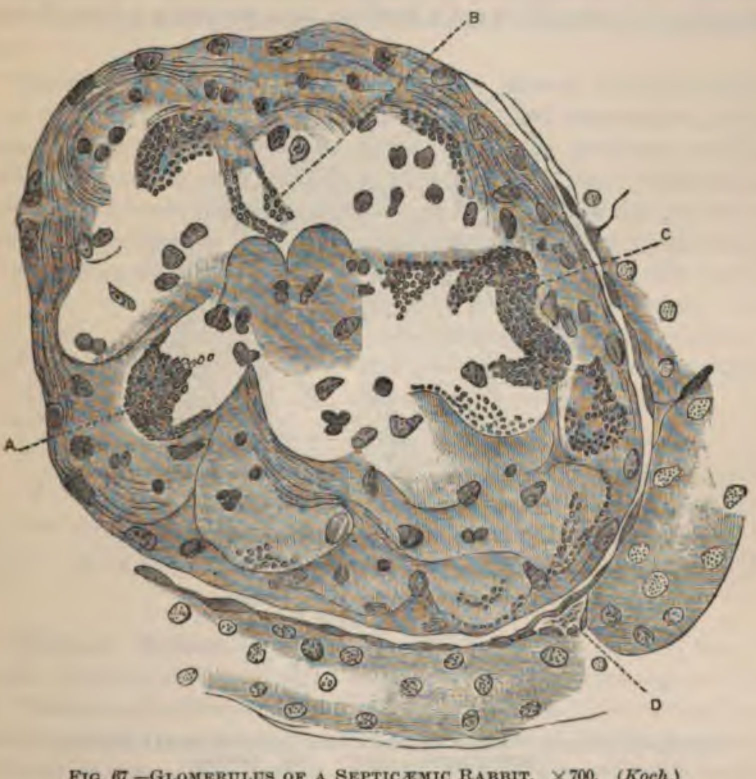

FIG. 67.—GLOMERULUS OF A SEPTICÆMIC RABBIT. ×700. (*Koch.*)

A, capillary loop with oval micrococci spread out like a membrane; B, micrococci deposited on the walls of a capillary vessel; C, loop completely filled with micrococci; D, individual micrococci in a capillary vessel near a glomerulus.

At many points these were so extensive that branching accumulations were seen consisting entirely of these organisms. This microbe was never seen to inclose blood-corpuscles, and, as they did not cause coagulation of the blood, embolism was never observed. The virulence of the bacillus was not increased by successive inoculation with infected blood from animal to animal. The bacillus now under consideration appears to be closely allied or identical with that of Davaine's septicæmia, which was first produced by injecting rabbits with putrid ox-blood. The two diseases are distinguished in that Davaine's septicæmia is easily transmissible to guinea-pigs, but not to birds; while mice, pigeons, fowls, and sparrows are very susceptible to the bacillus of septicæmia in rabbits, discovered by Koch, but guinea-pigs, dogs, and rats resist. Hueppe believes that this microbe is not a bacillus, but a coccus in a state of elongation; and Gaffky, Schuetz. Kitt, Salmon, Fluegge, and Baumgarten classify it with the bacilli. It readily stains in aniline solutions. Upon sterilized gelatin it grows in the form of clear, finely-granular drops, which, when they become confluent, form a culture which appears as a grayish-white film with jagged borders. Liquefaction of the gelatin never takes place. It can also be cultivated upon agar-agar, coagulated blood-serum, and potato. Gaffky investigated Davaine's septicæmia experimentally. He procured the infection by using water from a stagnant rivulet, and, by continually controlling the experiments with the microscope, using

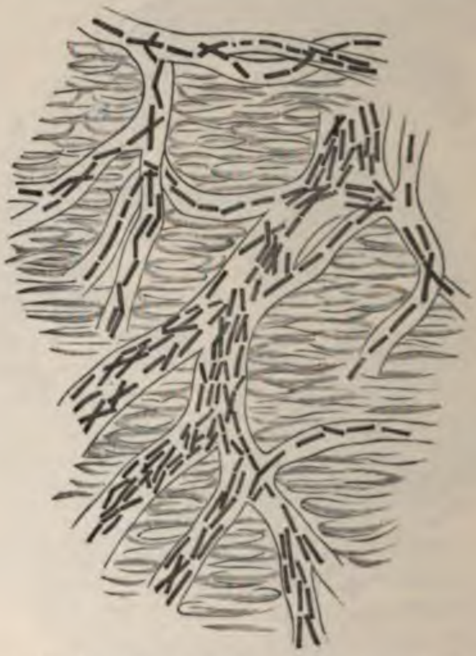

FIG. 68.—CAPILLARY VESSELS SURROUNDING THE INTESTINAL GLANDS OF A SEPTICÆMIC RABBIT. ×700. (*Koch.*)

Koch's methods, and working only with pure cultures, he was able to prove beyond a doubt that the theories of progressive virulence of bacteria were untenable. He showed that the highest degree of virulence was already attained in the second generation. He pointed out that the fallacious conclusions were due to impurification in the experiments, and that when the proper precautions are taken, in the process of sterilization, to prevent the admixture of other micro-organisms, the introduction of one kind always produces in the same animal the same definite result.

The most interesting conclusions to be drawn from the experiments in Koch's laboratory point to the fact that septicæmia is only a general term which includes a number of morbid processes, and this is well illustrated by the injection into the tissues of the "vibriones septiques" of Pasteur. Surface inoculations with these bacilli produce no effect; their pathogenic influence became only evident after injections into the subcutaneous connective tissue. Gaffky found that this bacillus grows most readily upon potato. Koch applied to the condition produced by this bacillus the term "malignant œdema."

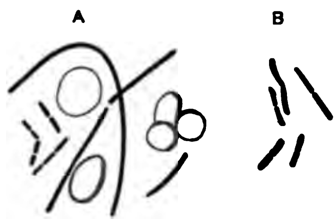

FIG. 69.—BACILLUS OF MALIGNANT ŒDEMA. × 700. (*Koch.*)

A, from the spleen of a guinea-pig; B, from the lung of a mouse.

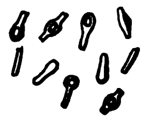

FIG. 70.—SPORE FORMATION IN BACILLUS OF MALIGNANT ŒDEMA. (*Fluegge.*)

Malignant Œdema.—The bacillus of malignant œdema was described by Koch as the cause of a fatal disease in guinea-pigs and rabbits. The same bacillus was described by Pasteur as "vibrion septique." Recently, this disease has been found also in some of the domestic mammalia and in man. The bacillus resembles morphologically the bacillus anthracis.

Usually, two or three bacilli are joined end to end, and thus form straight or curved rods two or three times the length of one bacillus. When stained, the threads present a granular appearance, from the unequal distribution of the staining material.

This bacillus is somewhat narrower than the anthrax bacillus, and when stained does not present such a regular, chain-like appearance. Sometimes the bacillus is found motile, but not always, while the anthrax bacillus is always devoid of this property. It multiplies by spores, but these appear only in the middle and at the ends.

This microbe is anaërobic, and can only be cultivated by exclusion of oxygen. The bacillus can only grow in the interior of agar-agar, gelatin, or coagulated blood-serum, if the needle-puncture on the surface of the nutrient medium is hermetically sealed. The growth of the bacillus is attended by the formation of gas-bubbles.

The gas has an intensely offensive odor. Blood-serum is liquefied. The temperature of the blood is most favorable to the growth of the bacillus, and cultures develop also, but slowly, at a temperature of 18° to 20° C.

This bacillus is widely diffused, and can be found in almost any putrefying substance. The bacillus of malignant œdema possesses the power of peptonizing albumen. It is found in abundance in garden-earth and hay-dust. If a small quantity of either of these substances is inserted underneath the skin of a guinea-pig, death is produced within forty-eight hours. The most characteristic post-mortem appearance is a diffuse œdema at the point of inoculation. The œdema-fluid is a clear, reddish serum, in which can be found bubbles of gas and numerous bacilli. The spleen is enlarged, of a darker color than normal, but the other organs present no macroscopical changes. The bacilli can be found in the parenchyma-fluid of nearly all organs, and especially is their number great in the envelopes of the infected organs. Mice die in from sixteen to twenty hours after inoculation. Horses, sheep, and pigs can be successfully inoculated, while cattle are immune to the bacillus. The disease can be communicated from animal to animal by implantation of fragments of infected tissue or by inoculation with 1 or 2 drops of the œdema-fluid. Surface inoculation is harmless, as the bacillus will not multiply when exposed to atmospheric air. In man malignant œdema appears in the form of progressive gangrene with emphysema (*gangrène gazeuse*). Recently, the identity of this disease with malignant œdema has been proved by inoculation experiments by Chaveau, Arloing, Brieger, and Ehrlich. Animals which have recovered from an attack of malignant œdema remain immune to this disease, but prophylactic inoculations have so far yielded only negative results. Chaveau made many experiments on guinea-pigs, sheep, and horses by injecting the liquid contents of bullæ which he found in cases of septic gangrene.

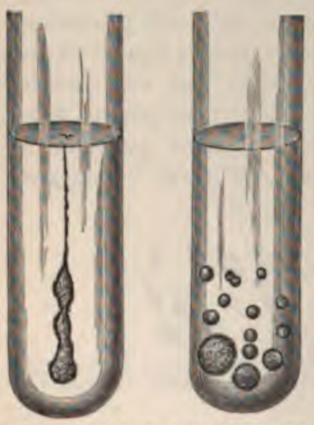

FIG. 71.—CULTURES OF BACILLUS OF MALIGNANT ŒDEMA IN GELATIN. (*Fluegge.*)

In doses of ⅙ drop in guinea-pigs and from 2 to 4 drops in horses, it produced death in a short time. In all cases the necropsy showed, at the point of injection, localized œdema and turbid serum in the peritoneal, pleural, and pericardial cavities. In the fluids the bacillus could always be demonstrated under the microscope. The disease could be reproduced in other animals by inoculation with the serous fluid contained in any of the serous cavities. The microbe proved less virulent when injected directly into the circulation.

PYOGENIC MICROBES AS A CAUSE OF SEPSIS.

The general symptoms which accompany all suppurative affections represent, etiologically and clinically, a form of sepsis, which differs in its intensity according to the quantity of pus-microbes, or their ptomaines, which reach the general circulation. The slight fever which often attends the development of a furuncle ceases with the removal of the products of inflammation, while a septic or diffuse suppurative peritonitis results in death in a short time from septic infection. The different forms of suppurative inflammation result in gangrene if the disease prove fatal; the immediate cause of death is usually septic infection or putrid intoxication. Watson Cheyne maintains that the microbes of sepsis only grow *in loco*, and act by producing toxic ptomaines, or, if they occur in the blood, they do not make emboli.

Vidal reported to the *Académie de Médecine de Paris* the results of his studies of the "forme septicemique pure" in puerperal fever of typhoid type without suppuration. In all of the cases in which he made a bacteriological examination he found the streptococcus pyogenes, and from this and the results of his culture and inoculation experiments he comes to the conclusion that it is impossible, in the present state of our knowledge, to distinguish between the various forms of streptococci, and that one and the same kind can set up any of the various forms of septic infection. Besser has examined 22 cases of traumatic sepsis, and found microbes of suppuration in every one of them. During the patient's life he discovered the microbe (*a*) in the blood in 4 of 16 cases examined; (*b*) in the pus or fluid discharge from the primary focus, in 17 of 17; (*c*) in the urine, in 3 of 4; and (*d*) in the sputa, in 3 of 3; while after death the micro-organism was present (*a*) in the blood, in 7 of 15; (*b*) in the internal organs, in 16 of 18; and (*c*) in the pus or uterine discharges, in 12 of 12. In 6 of 22 cases pus-microbes were simultaneously detected side by side with masses of bacteria of many other species. In 3 cases, however, the streptococcus was found alone, unassociated with any other microbe. Besser is of the opinion that the streptococcus of suppuration is the most frequent cause of sepsis. Smith isolated and cultivated, from 2 cases of puerperal sepsis, a streptococcus which, by inoculation and cultivation experiments, differed from the streptococcus of Fehleissen and the ordinary streptococcus of suppuration. He made a series of gelatin cultures with blood taken from the heart. After an interval of two or three days numerous colonies appeared. Rats inoculated with a pure culture died in from three to four days; the same microbe was discovered in their blood. Inoculations were also made in the ears of rabbits, and at the end of twenty-four hours a circumscribed redness without tendency to diffusion was apparent, the redness disappearing in two or three days. Another series of cultures and inoculations was made with blood taken from the finger of a woman sick with puerperal fever, with similar results.

From these considerations it becomes evident that the essential bacterial cause of septicæmia is variable, and that the disease represents a general febrile condition, which is brought about by the absorption from a local focus of different toxines from as many different microbes. As the introduction into the circulation of the products of putrefaction is followed by a complexus of symptoms which closely resembles what is understood clinically by the term septicæmia, and as different microbes have been cultivated from septic patients, it would seem that *this disease can be produced by any of the microbes which, after their introduction into the organism, have the capacity to produce a sufficient quantity of phlogistic ptomaines to give rise to septic intoxication.*

CLINICAL FORMS OF SEPTICÆMIA.

A clinical description of septicæmia cannot be given without a subdivision of the disease upon an etiological basis. Since the publication of Gaspard's researches it is absolutely necessary to make a distinction between septic intoxication and septic infection. By septic intoxication is understood that form of septicæmia which is caused by the absorption from a local focus of a ferment or the products of putrefaction, while the term septic infection is limited to those cases where septic micro-organisms gain entrance into the circulation, and not only exercise their pathogenic properties in the blood, but retain their capacity of reproduction in the circulation and distant organs. *Septic intoxication is caused by the absorption of a preformed ferment or toxine, which produces the maximum result as soon as it reaches the circulation, and the symptoms subside with the arrest of further supply and the elimination of the septic material from the circulation. Septic infection, on the other hand, occurs in consequence of the introduction into the circulation of living micro-organisms which multiply with great rapidity in the blood,—a circumstance which imparts to this form of septicæmia its progressive character.*

Septic intoxication is caused either by the absorption of fibrin ferment or the products of putrefactive bacteria.

(a) **Fermentation Fever.**—Fermentation fever (Bergmann), after-fever (Billroth), aseptic fever (Volkmann), resorption fever, are terms used to designate a general febrile disturbance caused by the absorption of the products of aseptic tissue necrosis. This, the most simple and harmless of all wound complications, appears as a temporary fever soon after an injury or operation, and is caused by the absorption of aseptic phlogistic substances. Different aseptic inert substances, when injected into the circulation, are known to produce a rise in temperature. Bergmann witnessed such a reaction after intra-venous infusion of a physiological solution of salt; Freese, after transfusion of blood of healthy animals; and Bergmann, Stricker, Albert, and Billroth, after intra-venous injections of a considerable quantity of well-water. The same effect is produced by intra-venous injections of water in which fine foreign particles, as flour or finely-pulverized charcoal, are suspended. Volkmann and Genzmer observed a rise in temperature in patients soon after the operation was completed and when the wound remained aseptic throughout, and hence called this form of fever aseptic fever. These authors attribute the fever to the reception into the blood of dead tissue material. Bergmann devised the term fermentation fever upon the theory that the fever is caused by the presence of fibrin ferment in the blood.

Augerer and Edelberg demonstrated experimentally that this fever occurs after transfusion, if the blood transfused contain fibrin ferment. Schmiedeberg attributed the fever to the presence of another blood ferment which he discovered and which he called "histozym." Bergmann and Augerer's experimental researches show that a fever which resembles the fermentation fever almost to perfection can be artificially produced in animals by intra-venous injections of pancreatin, pepsin, and trypsin. It would appear that the albuminoid substances, which are in excess in the blood, undergo oxidation by the action of a ferment, and that the chemical changes brought about in this manner occasion rise in temperature, while the products of oxidation are eliminated through the kidneys. Riedel found, in many cases of simple subcutaneous fracture, albumen in the urine during the first three or four days, and the urine always contained brown masses, which he regarded as products of the red blood-corpuscles. Worm Müller found invariably, after transfusion of blood, a considerable increase of urates in the urine. The occurrence of fever after the introduction of foreign aseptic substances into the circulation, can only be explained upon the supposition that they destroy red and white corpuscles in the blood, and that in this manner fibrin ferment, the cause of the fever, is generated.

Symptoms and Diagnosis.—Fermentation fever is prone to follow an operation or injury if antiseptic solutions are allowed to remain in the wound, thereby causing necrosis of the superficial tissues, or where, after closure of the wound, parenchymatous oozing gives rise to tension,—a local condition which forces the products of coagulation necrosis into the circulation. As not all extravasations of blood give rise to fever, we must take it for granted that when fever is not produced its absence is owing either to an absence of fibrin ferment or the existence of local conditions which prevent its absorption. From my own observations I am convinced that the amount of extravasated blood holds no relation whatever to the frequency of its occurrence or its intensity. A small extravasation under high pressure is more frequently the cause of fermentation than a large blood-clot in a location less favorable to the absorption of fibrin ferment. Fermentation fever makes its appearance within a few hours after an injury or operation, and, as a rule, it is not preceded by a chill. The temperature rapidly reaches its maximum, which varies from 100° to 104° F., and remains, without much variation, in the vicinity of the maximum height, to drop suddenly to normal at the end of the first to the third day. The pulse is correspondingly increased in frequency during the febrile attack. The sensorium remains intact, the appetite is not much disturbed, and none of the subjective symptoms are proportionate to the severity of the febrile disturbance. Patients with a high temperature feel so well that, if their wounds permit it, they will insist in walking around and will attend to their business, contrary to the advice of the attending surgeon. The most important diagnostic features of fermentation fever are its early onset after an injury or operation, and its spontaneous subsidence in from one to three days. As the disease is caused by the introduction of phlogistic substances from a local focus, and propagated by intra-vascular chemical changes, it is uninfluenced by any form of medication. The fever subsides spontaneously upon cessation of the primary cause, and with the elimination through the kidneys of the products of intra-vascular chemical changes. As the remaining forms of sepsis usually appear at a time when fermentation fever has run its course, the differential diagnosis presents no great difficulties.

The treatment of fermentation fever is entirely of a prophylactic nature. The prophylactic measures consist in a careful hæmostasis, and in cases where parenchymatous oozing, from the nature of a wound or the anatomical structure of the tissues, is to be expected, the prevention of the accumulation of the primary wound-secretion by efficient drainage. Fermentation fever must be included among the septic diseases, as the fibrin ferment acts as a toxic substance in the same manner as the toxines elaborated by septic micro-organisms. Future research may yet demonstrate that even this, the most harmless form of septicæmia, is not an aseptic fever, but that it is caused by pathogenic micro-organisms, either too few in number or not of sufficient potency to produce the graver forms of the disease.

(b) Sapræmia.—This word was devised by Mathews Duncan to include a form of septicæmia resulting from the absorption of the products of putrefaction. Sapræmia is the typical form of septic intoxication, as it is always caused by the introduction into the circulation of preformed toxines or ptomaines elaborated in dead tissues by putrefactive bacteria. It is closely allied to fermentation fever, as the symptoms are never intensified after the removal of the primary cause, but, as a rule, subside promptly after this has been accomplished. As sapræmia never occurs without putrefaction of necrosed tissue, and as putrefaction never takes place without infection with putrefactive bacteria, it becomes necessary to consider briefly the micro-organisms which are known to cause the clinical forms of putrefaction.

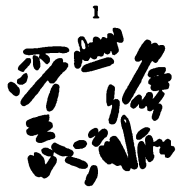

FIG. 72.

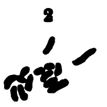

FIG. 73.

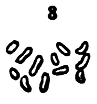

FIG. 74.

FIGS. 72, 73, AND 74.—BACILLUS SAPROGENES 1, 2, 3. 962:1. (*Rosenbach.*)

Bacilli of Putrefaction.—The bacilli of putrefaction exercise their pathogenic qualities only in dead tissue exposed to the atmospheric air. Clinically they are therefore present in the products of coagulation necrosis, or as a secondary infection in tissues destroyed by other micro-organisms. Most of them possess gasogenic properties. Rosenbach discovered, in different fetid secretions, three forms of bacilli which he designated respectively bacillus saprogenes 1, 2, 3.

Bacillus Saprogenes 1.—A comparatively large bacillus, which multiplies by end spores, which, however, grow only from one end of the bacillus.

On nutrient agar-agar the bacillus grows in the form of an irregular sinuous streak, with a mucilaginous appearance. The bacilli grow readily also in blood-serum, and all cultures emit the odor of decomposing kitchen refuse. Albumen or meat acted upon by a culture of this bacillus undergoes rapid putrefaction if exposed to atmospheric air, but if air is excluded the action of the microbes upon these substances is very slight. Cultures injected into healthy tissues and joints are harmless.

Bacillus Saprogenes 2.—This bacillus was isolated by Rosenbach from fetid sweat. The rods are shorter and thinner than the preceding ones.

This bacillus develops very rapidly on agar-agar, forming transparent drops, which become gray. The culture yields a characteristic fetid odor, similar to the last. Cultures of this bacillus injected into the knee-joint and pleural cavity of rabbits caused acute suppurative inflammation and death.

Bacillus Saprogenes 3.—This bacillus was discovered by Rosenbach in the pus of 2 cases of osteomyelitis with septic manifestations complicating compound fracture.

Cultivated on nutrient agar-agar, an ash-gray, almost liquid culture is developed, with a strong, characteristic odor of putrefaction. Injected into the knee-joint or abdomen of a rabbit, an opaque, yellowish-green infiltration resulted.

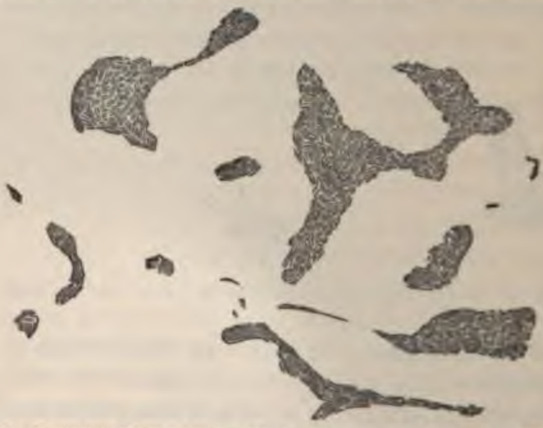

FIG. 75.—PROTEUS VULGARIS. 285:1. SWARMING ISLETS. (*Hauser.*)

Proteus Vulgaris.—This and the following species have been recently described by Hauser as present in putrefying meat-infusions, and as being intimately connected with the process of putrefaction. As the name indicates, these bacteria are capable of changing their form during their development. The different species of proteus have been described as coccoid, bacteroid, spindle-shaped, and spiralinar, on account of the ever-changing form they assume during their growth. In proteus vulgaris the bacteria vary greatly in size.

Many of the rods are actively motile, and cultivated upon nutrient gelatin they convert it into a turbid, grayish-white liquid. If cultivated in a capsule containing 5 per cent. of nutrient gelatin, a few hours after inoculation, the most characteristic movements of the individual bacilli are observed on the surface of the gelatin, although at this early stage no liquefaction can be detected. The movements are not observed if the nutrient medium contains 10 per cent. of gelatin. Spore formation was never observed. Injected subcutaneously in small doses, no results were obtained; larger doses sometimes caused circumscribed abscess at the point of injection. Intra-venous injection of a large dose produced toxic symptoms in rabbits and guinea-pigs, and these were not modified by using the filtrate of a liquefied culture, showing that the toxic substance was held in solution.

Proteus Mirabilis.—Rods varying greatly in length, sometimes so short that they appear like cocci, at others of considerable length.

The rods occur singly and in zoöglœa, and sometimes in tetrads, pairs, chains, or as short rods in twos, resembling bacterium termo,—in fact, in all conceivable transition forms.

Cultivated on nutrient gelatin they form a thick, whitish layer, in concentric circles, which in time liquefies the medium. Similar movements are observed in capsule-cultivations as with proteus vulgaris. The pathogenic properties of the mirabilis are the same as those of vulgaris.

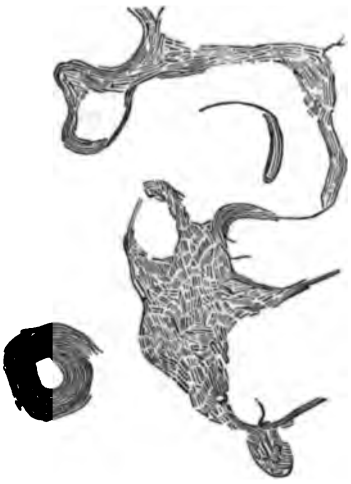

FIG. 76.—PROTEUS MIRABILIS. 285:1. SWARMING ISLETS. (*Hauser.*)

Proteus Zenkeri.—Rods about four times as long as wide, in two, like bacterium termo. Cultivated on nutrient gelatin no liquefaction results, but a thick, whitish-gray layer is formed, with sloping margins. The bacilli are motile, and the same phenomena are observed on the solid medium as in the other forms. Spirilli and spiralinar forms are seldom seen. Gelatin and blood-serum cultures emit no fetid odor, but meat-infusion undergoes rapid putrefaction and yields the usual fetid odor. The pathogenic qualities are the same as those of the other species of proteus.

As the microbes of putrefaction, which have first been described, possess limited or no pathogenic qualities when introduced into healthy tissue, it is evident that their toxic effect is caused by a soluble substance which they produce when they find their way into dead tissue exposed to atmospheric air. This leads us to a consideration of the

Ptomaines.—Ptomaine is a term used to designate certain toxic substances (resembling alkaloids) which are produced during the process of putrefaction. Gautier has shown that in dead animal tissues processes of putrefactive decomposition set in, by which certain alkaloids are elaborated from albuminous substances, which have been called ptomaines by Selmi. In the latter part of the seventeenth century Kircher and Leuwenhoek claimed that putrid substances contained minute microscopical worms, which caused the putrefaction. In 1820 Kerner pointed out the resemblance between the symptoms of poisoning by sausages and by atropine. He was thus the first to raise the suspicion that toxic alkaloids were formed through the decomposition of albumen. In 1856 Panum showed that the inflammatory change which occurs in the intestinal mucous membrane of animals fed on putrid infusions is due to a chemical poison, which remained unaffected by boiling for a long time; and his conclusion that the toxic substance contained in putrid fluids was of a chemical nature was confirmed by Weber, Hemmer, Schweninger, Stich, and Thiersch. In 1875 W. B. Richardson isolated a toxic substance, which he called "septine," from the inflammatory transudation in the peritoneal cavity of a person that had died of pyæmia. With this substance he successfully infected animals. He also found that this substance could be made to combine with acids, so as to form salts, without losing its toxic qualities. Bergmann and Schmiedeberg isolated a crystalline poison from decomposing yeast, to which they gave the name of "sepsin." This substance, when injected into the subcutaneous tissue or venous circulation in animals, produced well-marked symptoms of septic intoxication; the intensity of the symptoms were found to vary with the amount of the substance injected. Zuelzer and Sonnenschein obtained, from macerated dead bodies and from putrid meat-infusions, small quantities of a crystallizable substance which exhibited the reactions of an alkaloid, and had a physiological action like atropine, dilating the pupil, paralyzing the muscular fibres of the intestine, and increasing the rapidity of the pulse. In 1857, Pasteur made the important discovery that specific micro-organisms

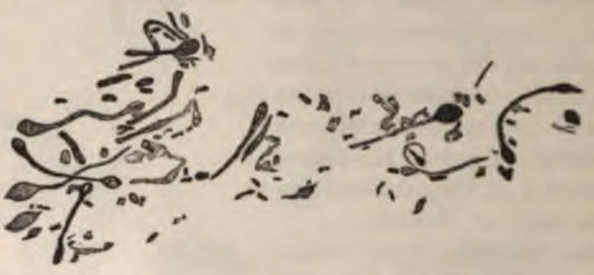

FIG. 77.—INVOLUTION FORMS OF PROTEUS MIRABILIS. 524:1. (*Hauser.*)

are the cause of the various forms of fermentation and putrefaction. No discovery, perhaps, attracted such universal attention as Pasteur's theory of fermentation. This theory was strengthened somewhat later by Lemaire's observation, that all fermentative changes in fluids are suspended on the addition to the fluids of phenic acid, from which he concluded that fermentation must be due to living organisms. Next came the carefully-conducted experiments of Lister, who showed that air is deprived of its action in causing putrefaction of organic substances if it is passed through a filter, or if the fluids are placed in an open vessel with the mouth of the vessel so arranged that dust cannot reach the fluid by gravitation.

Lister's great life-work, antiseptic surgery, that has created a new epoch in the history of medicine and surgery, is based upon what then was still a theory, that inflammation, suppuration, and septic infection of wounds are caused by living specific micro-organisms. Selmi discovered ptomaines in an exhumed body, in 1872. The ptomaines isolated by him were volatile alkaloids. Gautier, independently of Selmi, and about the same time, made the same observations, but believed that the toxic substances were volatile, and that in their action they resembled the narcotics, morphia and atropia, and were more nearly allied to the alkaloid extracted from poisonous mushrooms.

Semmer gives an account of the action of septic substances as studied experimentally by Guttmann, of Dorpat. The experiments were made with putrid substances, products of inflammation, septic blood, and cultivations of septic bacteria. These researches showed that a chemical poison is formed in putrefying substances, and that a certain quantity of such poison produces symptoms of sepsis and death in animals. The blood of animals killed with such putrid poisons was found to possess no infective qualities, and the usual putrefactive bacteria were destroyed in the blood, and only appear again after the death of the animal. It was claimed, even at that time, that the bacteria elaborate the poison, as experiments made with cultures grown outside the body produced the same effect. Another conclusion arrived at was that putrid substances administered subcutaneously may produce gangrene, phlegmonous inflammation, or erysipelas, according to the stage of putrefaction, temperature, culture-soil, etc. The infective material was never found in the blood, but always in the products of inflammation. It was clearly stated that true septicæmia is always preceded by a stage of incubation, and that its contagium is destroyed by boiling, putrefaction, and germicides.

Bergmann and Augerer produced a condition in animals resembling septicæmia, by injecting into the circulation pepsin, pancreatin, and trypsin. When death occurred after intra-vascular injections of these ferments, fibrinous deposits were found in the heart and pulmonary vessels. These experiments were, therefore, confirmatory of the observations previously made by Edelberg and Birck, who had shown that the injection of putrid substances into the circulation materially increased the free fibrin ferment in the circulating blood.

Blumberg concluded, from his numerous experiments on animals, that the symptoms which follow an injection of putrescent material into the circulation are not always constant; that, in fact, extreme prostration, high temperature, rapid pulse and respiration are the only constant symptoms found. The same author also confirmed the statement that the blood of patients dying from putrid intoxication contained no micro-organisms. Samuel maintains that putrid fluids, from the second day until the eighth month of putrefaction, act differently, and divides their action according to this supposition into three stages: 1. *Phlogogenic*, in which they produce only inflammation. 2. *Septogenic*, in which they produce in the living organism putrefactive processes. 3. *Pyogenic*, in which they cause only suppuration, having lost in the meantime their other pathogenic qualities.

Mikulicz found that putrid fluids, according as they are free from bacteria or contain more or less of putrefactive microbes, will produce a slight inflammation, a suppurative inflammation, or a progressive phlegmonous inflammation. Fränkel detected but few micrococci in the blood of septicæmic patients, and observed that they greatly increased after death; but, after the lapse of some further time, altogether disappeared, thus also confirming a fact previously known, that putrefaction destroyed septic microbes. These observations may tend to harmonize the discrepancy of opinion, growing out of the different results obtained by different experimenters, by injections of putrid substances, as some of the fluids may have contained an abundance of living micro-organisms, while others may have been rendered sterile by age, owing to advanced putrefactive changes. Brieger and Maas have rendered valuable service in the chemical isolation of ptomaines, or, as Brieger calls them, toxines, from putrid substances, and the results of their inoculation experiments established more firmly the fact of putrid intoxication by these soluble alkaloid substances. The number of bacteria in rabbits killed by septic infection is so great that death may ensue from simple mechanical causes, while in fatal cases of sepsis in man the number is often so small that it seems natural to suppose that the micro-organisms are capable of producing some poisonous substance, which destroys the patient before they have time to multiply to the extent observed in septicæmia in rabbits and mice.

Rinne asserts that the chemical products of pus-microbes alone, as well as sterilized putrid fluids, never produce metastasis. He sterilized fluid cultures of the staphylococcus pyogenes aureus after filtration, and injected directly into the blood-vessels of rabbits as much as 4 grammes of this fluid, and in dogs increased the dose to 14 grammes. Many of the animals showed slight symptoms of septic intoxication, somnolence, diarrhœa, and collapse. By using still larger doses the symptoms were intensified and the animals died from well-marked symptoms of septic intoxication. Metastatic abscesses were never found in these cases. The same author has recently published some very interesting observations on the immediate cause of death in rabbits inoculated with a pure culture of Koch-Gaffky's bacillus. The animals were inoculated at the base of the ear, and immediately after death the ptomaines were isolated from the tissues by Brieger's method. In every instance he obtained a substance called methylguanidin, which on chemical analysis was shown to consist of the formula $C_2H_7N_3$. When this substance was injected into rabbits it produced symptoms of septic intoxication which resembled, in every particular, those produced by the injection of pure cultures obtained from septicæmic rabbits. As methylguanidin could not be produced from the cadavers by the same method, Hoffa naturally came to the conclusion that it was a product of the bacilli, and that death was to be attributed to the production of this toxic substance in the tissues of the infected animals by the specific action of the bacilli. The source of methylguanidin in the body is kreatin, and the bacteria must possess the property of oxidation, as kreatin is transformed into methylguanidin only by oxidation. Brieger has isolated from human corpses a different set of toxic alkaloids, one of which he calls "cadaverin" and the other "putrescin," which are but feeble poisons; while two others, "madeleine" and "sepsin," which are produced later on in the decomposition, are much more powerful poisons, causing paralysis and death. From decomposing albuminous substances he has obtained many other well-defined chemical bodies, as well as some substances to which no names have yet been given.

Bourget isolated several toxic bases from the viscera of a woman who had died of puerperal sepsis. He also obtained from the urine from patients suffering from the same disease similar toxic bases, which killed frogs and guinea-pigs, when administered by injection, showing that the toxic substances formed during life, and that they are eliminated through the kidneys.

The experimental and clinical researches to which I have referred above show conclusively *that septic intoxication is caused by the presence of dead tissue in the body in a state of putrefaction, from the presence* *of putrefactive bacilli, and that the immediate cause of the intoxication is the absorption of preformed ptomaines from such a local focus of putrefaction.*

Symptoms and Diagnosis.—Septic intoxication sufficient in severity to give rise to grave general disturbances is usually initiated by a chill, or at least by a sensation of chilliness, followed by a continued form of fever, the temperature rapidly increasing to 102° to 104° F., with slight morning remissions. The character of the pulse furnishes the most reliable information in regard to the intensity of the intoxication. All ptomaines of putrefactive bacteria exert a depressing influence on the heart; hence the force and frequency of the pulse furnish important diagnostic and prognostic evidences. The pulse is always soft and compressible,—qualities which indicate diminished intra-vascular pressure, resulting from an enfeebled *vis a tergo.* Complete loss of appetite, vomiting, and diarrhœa are almost constant symptoms in grave cases. The tongue is usually furred, dry, and, in severe cases, presents the "dried-beef" appearance. The urine is scanty and heavily loaded with urates. Headache is often complained of in the beginning of the attack. Delirium, restlessness, insomnia, are symptoms which denote approaching danger. Subsultus, dilatation of pupils, clammy perspiration, livid appearance of visible mucous membranes, low-muttering delirium, involuntary discharges, coldness of the extremities, fluttering, and feeble pulse precede death from septic intoxication. One of the most important elements in the diagnosis is the detection of a local focus of putrefaction. As the putrefaction always occurs in parts of the body exposed to the atmospheric air, its existence can readily be ascertained by the sense of smell. The intensity of the fœtor of the gases produced by the putrefactive bacteria varies greatly, but the smell is always suggestive of decomposing meat or kitchen refuse. The impression is quite prevalent, not only among the laity, but also in the profession, that the local lesions which cause septicæmia always emit a fetid odor. *This is a grave mistake. Fœtor is associatad with putrefaction, and as such is suggestive of sapræmia, and not true progressive sepsis.* The latter may be combined with sapræmia, but when it occurs independently of this no bad smell can be detected, and yet it is the most fatal form of sepsis. In reference to the differential diagnosis between sapræmia, fermentation fever, and septic infection, it must be remembered that septic intoxication can only occur from putrefaction, and therefore three conditions must invariably be present in the etiology of this form of sepsis: 1. Dead tissue. 2. Infection of this dead tissue with putrefactive bacteria. 3. A sufficient length of time must have elapsed since the injury or operation for the putrefactive bacteria to produce a toxic quantity of ptomaines to cause symptoms of intoxication. The dead tissue may be a blood-clot in a wound, around the fragments of a compound fracture, or in the interior of the uterus; it may be tissue devitalized by a trauma, heat or cold, the action of chemical substances, or the action of bacteria other than putrefactive; or it may be detached, retained fragments of placental tissue. That such dead tissue has become the seat of infection with putrefactive bacteria can be ascertained by the presence of fœtor and bubbles of gas. At the temperature of the body putrefaction progresses very rapidly; but a differential diagnosis can generally be made without much difficulty, between sapræmia and fermentation fever, by the time which has elapsed between the injury or operation and the manifestation of the first symptoms of septic intoxication. Fermentation fever appears within a few hours, certainly always before the end of the first day, while septic intoxication from putrefaction seldom begins before the expiration of twenty-four hours. If septic infection begin during this time it is not attended by any evidences of putrefaction.

Prognosis.—Uncomplicated sapræmia proves fatal by the absorption of a deadly dose of ptomaines from a local depot of putrefaction, and the prognosis will therefore depend upon the stage of intoxication and the feasibility of the removal of the infected dead tissue by surgical treatment. If an efficient, radical treatment can be instituted at a time before a fatal dose of toxic substances has reached the general circulation, the prognosis is favorable. A decomposing blood-clot or detached fragment of a placenta can be readily removed and the field of operation sterilized. The prognosis in sapræmia complicating progressive gangrene is always grave, as the dead tissue is increased by other microbes; hence the conditions created by both kinds of microbes are of a progressive character.

Treatment.—The prophylactic treatment of sapræmia consists in the removal of dead tissue, prevention of subsequent extravasation and accumulation of blood by careful hæmostasis,—if necessary, by drainage,—and finally sterilization, by antiseptic measures, of dead tissue that cannot be removed. Iodoformization of dead tissue is an excellent means of preservation. In the extra-peritoneal treatment of the stump after supra-vaginal extirpation of the uterus, the same object is accomplished by touching the raw surface with a solution of perchloride or persulphate of iron or pure carbolic acid. Wounds in which dead tissue is unavoidably retained should always be treated by drainage. After symptoms of septic intoxication have developed early, radical treatment must be pursued. This treatment comprises the removal or sterilization of the dead tissue. A decomposing blood-clot is to be removed and the parts are thoroughly irrigated with a solution of corrosive sublimate, and re-accumulation prevented by efficient drainage. In cases of gangrene complicated by putrid intoxication, where it is impossible to remove the infected tissues by mechanical measures, and complete disinfection without such a procedure cannot be effected, the best results are obtained by permanent irrigation with a saturated solution of acetate of aluminum. Under this treatment the soluble toxic substances are washed away as fast as they are formed, and sterilization of the soil for the putrefactive bacteria is gradually accomplished by the saturation of the dead tissue with this safe and efficient antiseptic solution. If a suppurating cavity is the seat of putrefactive changes, it becomes necessary to remove the nutrient medium for putrefactive bacteria by first washing out the cavity with a strong antiseptic solution, to be followed by the mechanical removal of dead tissue, shreds of connective tissue, dead granulations, etc., by means of a sharp spoon or dull curette, and subsequently by another antiseptic irrigation. The surgical treatment of sapræmia will soon decide the fate of the patient. If a fatal dose of ptomaines has reached the general circulation before an effort is made to procure sterilization of a local depot of putrefaction the local treatment will, of course, prove unsuccessful in preventing a fatal result, and the disease will continue its relentless course uninfluenced by the treatment. If, however, the intoxication has not progressed to this extent, efficient local treatment is followed by the most brilliant results. Within a few hours after the sterilization of the local focus of putrefaction the temperature falls to normal, the pulse becomes slower and fuller. If the tongue has been dry it soon becomes moist; if the patient has been delirious consciousness returns, and the patient is convalescent in a few days. The results of the antiseptic local treatment in these cases are the strong contrast with the useless and often dangerous internal administration of antipyretics. The treatment directed toward the disinfection of the local focus of putrefaction removes the cause of the intoxication, while the antipyretics may effect a temporary reduction of the temperature, but at the same time, by diminishing the contractile power of the heart, only add to the danger by diminishing the resistance to the action of a depressing poison. The use of antipyretics in the treatment of sapræmia is strongly contra-indicated. All debilitating treatment must be carefully avoided as being unscientific and as adding to the existing dangers. The best results are obtained by such local treatment by which the further production of ptomaines is prevented, consequently *by measures which meet the etiological indications*. The debilitating effects of the ptomaines on the heart are met by the timely and judicious administration of stimulants. In urgent cases such diffusible stimulants as sulphuric ether, camphor, and musk can be administered with advantage subcutaneously, in order to gain time for the action of remedies which will have a more permanent effect on the heart. Digitalis, strophanthus, strychnia, and atropia in small doses are excellent cardiac tonics and stimulants, and are indicated in cases where the pulse is very rapid and soft, denoting a feeble peripheral circulation from a weakened heart. Where life is threatened from syncope the patient is not allowed to assume a sitting postion, for fear that the increased intra-cardiac pressure might result in sudden death from heart-failure.

Alcoholic stimulants are to be given in doses sufficiently large to improve the character of the pulse, and at sufficiently short intervals to maintain this effect without interruption. Brandy or whisky, in doses of an ounce every two hours, diluted with water, are most to be relied upon, but champagne, Greek sherry, or Reich's Tokayer are excellent substitutes. If the stomach is irritable or the symptoms are less urgent. concentrated liquid food, like beef-tea, milk, and eggnogg, must be given at regular intervals to assist the action of stimulants in sustaining the heart's action until sufficient time has been gained for the elimination of the ptomaines.

(c) Progressive Septicæmia.—This is the septic infection of modern authors, and differs from septic intoxication in that it is caused not by putrefactive bacteria, but by microbes which enter the circulation from some local septic focus, and which retain their capacity of reproduction in the blood. It is called progressive sepsis, because, only too often, it is not followed by any abatement of the symptoms, as the essential cause has passed beyond the reach of any local treatment, and goes on increasing in the blood until it destroys the patient. *The intoxication in this form of sepsis is not only caused by ptomaines which are produced at the primary seat of infection, but ptomaines are also produced in the blood by the microbes which it contains.*

True progressive sepsis is caused by the introduction of septic micro-organisms into the tissues, where they multiply and, later, reach the blood, where mural implantation and capillary thrombosis take place, which directly interfere with the proper nutrition and function of important organs, and where the septic intoxication is caused by the formation of ptomaines, both in the blood and living tissues. For this form of sepsis Neelsen has suggested the name of "acute mycosis of the blood," to distinguish it from putrid intoxication, which we have just described, and which Neelsen calls "toxic mycosis of the blood," in which few or no microbes are found in the blood, and in which death is due exclusively to the absorption of preformed toxic substances from a putrefying depot.

Causes.—Klebs discovered and described a microbe, the *mikrosporon* *septicum*, which he believed was the specific cause of septic processes, but recent researches seem to prove that the pus-microbes are the most frequent cause of progressive sepsis. The pus-microbes either reach the circulation directly by permeating the vessel-wall, or they enter by a more indirect route, through the lymphatic channels. The latter mode of infection gives rise to the most acute and fatal form of sepsis. In many cases of septic infection the presence of lymphangitis can be demonstrated during life, and by examination after death. A few years ago Bergmann advanced the theory that in septicæmia micro-organisms enter the colorless blood-corpuscles, and by multiplication within them cause their dissolution, a process during which the fibrin-generators are elaborated,—an occurrence ending in intra-vascular coagulation and capillary embolism. In Koch's septicæmia in mice such a chain of pathological conditions can be readily demonstrated, but in many cases of fatal sepsis in man the microbes found in the blood are few, no destruction of leucocytes can be shown to have occurred, and extravasations and capillary embolism are absent; hence death cannot be attributed to fibrin intoxication. *In such instances we can only assume the presence of a soluble ptomaine which is diffused throughout the entire body and destroys life by its toxic properties.* The formation of pus at the primary seat of infection is not necessary in the causation of septicæmia by pus-microbes. Septic infection is as liable to take place from wounds that do not suppurate as from suppurating wounds. Why a wound infected with pus-microbes should give rise to progressive sepsis in one individual, and suppuration or suppuration and pyæmia in another, does not admit of a satisfactory explanation at the present time.

Rinne has shown that diminution of the absorptive capacity of the tissues at the seat of infection plays an important part in the development of septic processes. If the pus-microbes are rapidly absorbed, destroyed in the blood, or removed by elimination, septic inflammation is prevented. If, on the other hand, the local conditions are such that the microbes remain in the tissues, and by their rapid multiplication produce a large amount of soluble toxines, which, when they reach the blood, not only produce intoxication, but prepare the blood and tissues for the localization and reproduction of the microbes at points distant from the primary seat of the infection, the pathogenic effect of the microbes on the tissues at the primary seat of infection diminishes their power of resistance, and the microbes either enter the blood-vessels directly or through the lymphatics. Experimentally it has been shown that if a large quantity of pus-microbes is introduced into the peritoneal cavity, or directly into the circulation, death results from sepsis before a sufficient length of time has elapsed for the pus-microbes to produce the histological changes which are necessary for the production of pus. *These experiments are strongly suggestive of the fact that, in man, infection with pus-microbes causes progressive sepsis, if a large quantity of pus-microbes is introduced into tissues debilitated by a trauma, antecedent pathological conditions, or the action of preformed ptomaines.* Under such circumstances the pus-microbes are reproduced with great rapidity at the primary focus of infection, enter the circulation before suppuration has had time to develop, and produce a complexus of symptoms and a series of pathological changes characteristic of progressive sepsis.

Symptoms and Diagnosis.—The most typical clinical picture of progressive sepsis is produced in cases of septic peritonitis, dissection wounds, puerperal septicæmia, and acute multiple osteomyelitis. In septic peritonitis, after laparotomy or penetrating wounds of the abdomen, the septic inflammation, as a rule, develops within the first forty-eight hours, and with it the characteristic symptoms of septicæmia appear. In puerperal sepsis and the gravest form of acute suppurative osteomyelitis, the septic symptoms often overshadow the primary disease to such an extent that this is entirely overlooked. Dissection wounds often prove fatal from septic infection, which spreads from the wound along the course of the lymphatic vessels, and finally becomes general through the medium of the circulation. Septic infection from an accidental or operative wound can take place within twenty-four hours, and seldom occurs later than the third or fourth day, unless the infection has taken place after the first dressing. Like all other acute infectious processes, septicæmia is ushered in by a more or less pronounced chill, or at least a subjective sensation of chilliness, which may be repeated during the first twenty-four hours. The chill is never so pronounced as in pyæmia, and does not return with the same regularity and intensity as in that affection. The chill announces the termination of the period of incubation, and is promptly followed by symptoms of reaction which, in their severity, are proportionate to the intensity and gravity of the attack. One of the most prominent features of the disease is a profound prostration, which may be well marked a few hours after the beginning of the attack. If septicæmia follow an operation, or a severe accident, it is sometimes almost impossible to decide whether the pronounced loss of strength should be attributed to shock, the use of an anæsthetic, or the beginning of an attack of septicæmia. One of the most delusive symptoms is the utter indifference of the patient, not only as to his own grave condition, but to all of his surroundings. This apathy is a characteristic symptom of profound septic intoxication. The patient complains of no pain. assures the physician and friends that he is feeling well, shows absolutely no anxiety concerning his own fate, and does not comprehend the anxiety of those around him. Drowsiness, bordering almost on stupor, is frequently observed. The face presents a pale or ashy-gray color, and in advanced cases it presents a yellowish, icteric tint, but the sclerotica always retains its white color. In the beginning of the attack the pulse ranges between 80 and 90 degrees, but becomes rapid, small, and compressible as the intoxication and capillary obstruction progress. The character of the pulse is of great diagnostic and prognostic importance. If the pulse within a short time reach a frequency of 140, and imparts the sensation as though the artery were only half filled with blood, it is a symptom which forebodes immediate danger. The temperature is variable. A subnormal temperature, with a rapid, feeble pulse, indicates a grave and probably fatal form of sepsis. If the temperature is at first only slightly increased, but gradually rises to 103° or 104° F., it denotes progressive sepsis. A high temperature and a firm pulse, not exceeding 120 beats to the minute, are indications of less serious import than a low temperature with a rapid, feeble pulse. The eyes are sunken, often suffused with an abundant secretion from the conjunctiva. The features present a stolid appearance, without any expression of intelligence. Capillary oozing at the primary seat of infection is a common occurrence, and capillary hæmorrhage underneath the skin and visible mucous membranes is frequently observed. Vomiting and diarrhœa are often present from the beginning, and in rapidly fatal cases remain as persistent symptoms, in spite of measures that may be employed to subdue them. The discharges from the bowels are often stained with blood. The urine, as a rule, is scanty and loaded with urates.

Billroth places great importance upon the appearance of the tongue. The tongue is always coated; in grave cases it is pointed at the tip, its margins are red, while the dorsal surface is dry and covered with a dry, often almost black, crust. Return of moisture is always a favorable omen. Great thirst and complete loss of appetite are always present. Delirium is a frequent, but not a constant, symptom. If the case progress to a fatal termination, the pulse becomes more and more frequent, respirations become shallow and labored, the face presents a cyanotic hue, the surface is bathed with a clammy perspiration, the extremities become cold, and death finally is caused from heart-failure. In the differential diagnosis it is important to remember fermentation fever, septic intoxication, typhoid fever, internal sepsis, and acute multiple suppurative osteomyelitis. Progressive septicæmia always has a stage of incubation; that is, a certain length of time intervenes between the time infection occurred and the appearance of the disease. This period of incubation may terminate at the end of a few hours and it may be prolonged to four days, according to the number of pus-microbes introduced and the anatomical structure and physiological properties of the tissues primarily infected. Fermentation fever follows an injury or operation within a few hours, and never occurs after the expiration of twenty-four hours. In fermentation fever the maximum symptoms appear at once, and the force of the pulse and strength of the patient remain unimpaired. Fermentation fever seldom lasts for more than one or two days, while in progressive sepsis the symptoms become aggravated as the infection increases. In putrid intoxication the maximum symptoms are produced by the introduction into the blood of preformed soluble toxic substances from a depot of putrefaction. Evidences of putrefaction in any part of the body would speak in favor of septic intoxication, while, if septic infection exist at the same time, it must be regarded not in the light of a cause, but as a complication. Typhoid fever is preceded by a well-marked prodromal stage which is absent in septic infection. The eruption in typhoid fever is characteristic, while the eruption which is sometimes seen in progressive sepsis closely resembles the rash of scarlatina, and is caused by the presence of pus-microbes in the superficial lymphatic vessels. Internal sepsis is usually preceded by a septic pharyngitis, and frequently attended by ulcerative endocarditis. Acute multiple osteomyelitis, the cause of fatal septic infection, can be recognized by searching for points of tenderness in the localities attacked most frequently by this disease. The final diagnosis of septic infection must be based upon the existence of an infection-atrium, through which pus-microbes have entered the tissues, and from which they have reached the general circulation.

Prognosis.—The prognosis of progressive septicæmia is always grave. In cases where pus-microbes exist in large numbers at the primary seat of infection, and reach the general circulation with great rapidity, and meet with conditions favorable for their reproduction, death is inevitable in spite of the most energetic local and general treatment. The prognosis is more favorable if infection has taken place from a locality amenable to thorough local disinfection, if this is practiced upon the first appearance of symptoms, as this treatment prevents further ingress of pus-microbes into the circulation. The existence of multiple points of metastatic inflammation renders a recovery improbable. Delirium, rapid and feeble pulse, subnormal temperature, dry tongue, persistent vomiting and diarrhœa are all unfavorable symptoms from a prognostic stand-point. Capillary hæmorrhages distant from the primary infection-atrium are infallible indications of progressive sepsis, and their existence warrants a most unfavorable prognosis. Progressive sepsis may cause death in twelve hours, and in fatal cases life is seldom prolonged for more than one week.

Pathology and Morbid Anatomy.—In rapidly-fatal cases of progressive septic infection, the absence of gross macroscopical pathological changes is a characteristic feature of this disease. In such instances even the most careful search for tangible lesions will result negatively. Cloudy swelling of the parenchyma of internal organs indicates the existence of coagulation necrosis, caused by the action of the ptomaines of the pus-microbes. Pus-microbes have been frequently found in septic blood. Hæmorrhagic extravasations into organs, and more particularly underneath serous and mucous membranes and the skin, are frequently present. The blood presents almost a black color, and shows little or no tendency to coagulate. The lymphatics interposed between the primary seat of infection and the blood-vessels are frequently found in a state of septic inflammation. The wound through which infection has taken place may present but slight or no gross anatomical changes. The spleen is enlarged and the pulpa softened to the consistency of a blood-clot. Thrombosis and embolism are absent. Under the microscope the capillary vessels everywhere present all the evidences of a septic inflammation. The soluble ptomaines in the blood produce coagulation necrosis of the intima, which determines mural implantation of the pus-microbes and the colorless corpuscles and results in capillary hyperæmia and congestion. In some places alteration of the capillary wall has taken place to such an extent as to give rise to rhexis. The most important microscopical changes in the tissues and organs, in patients who have died of sepsis, are the pathological conditions within and in the immediate vicinity of capillary vessels that indicate the existence of multiple foci of metastatic inflammation, which characterize clinically and pathologically progressive sepsis. If life is prolonged for a sufficient length of time, these foci become the centre of a suppurative inflammation. Slight effusions into the large serous cavities are frequently found.

Treatment.—The antiseptic measures which have been described in the treatment of wounds are the best and only known means of effective prophylaxis against septic infection. Any method or methods of treatment which can be relied upon in the prevention of suppuration will be found efficient in preventing septic infection. As retention of wound-secretion is one of the important etiological conditions in the causation of septic infection in wounds that are not completely aseptic, drainage should be employed in all cases where an accumulation of the primary wound-secretion is to be feared. As septic infection is just as liable to occur through a small as a large wound, the most insignificant injury should be treated upon the strictest and most pedantic antiseptic precautions. If, in spite of the greatest care, symptoms of septic infection appear after an injury or operation, no time should be lost by the useless administration of antipyretics, in the vain hope that by reducing the temperature the condition of the patient will be improved, but the first and essential object of treatment should be to remove the cause of the fever by resorting to secondary disinfection. All sutures must be removed and every portion of the wound rendered accessible to local treatment. Extravasated blood and necrosed shreds of tissue must be removed, when the wound is to be irrigated with a 1-to-1000 solution of corrosive sublimate, after which it is dried and the whole surface brushed with a 10-per-cent. solution of chloride of zinc. After another irrigation and after drying the surface again, a thin film of iodoform is applied, and then the wound is tamponed with iodoform gauze and dressed antiseptically. Such a wound should never be re-sutured until the local and general symptoms indicate that it has been rendered completely aseptic. If this secondary disinfection prove unsuccessful, recourse should be had to permanent irrigation with a saturated solution of acetate of aluminum. Secondary disinfection of the peritoneal cavity, in cases of septic peritonitis after laparotomy, has so far not proved very satisfactory, but as it is the only recourse in dealing with such desperate cases, that without it would surely run a fatal course in a short time, it should never be neglected. A number of the sutures near the lower angle of the wound are removed with blunt instruments, the margins of the wound are separated, and the abdominal cavity is flushed with warm salicylated water until the fluid returns perfectly clear. The end of the rubber tube attached to the irrigator must be inserted in such a manner that the stream will reach the most dependent portions of the abdominal cavity; hence it is inserted into the deepest portion of the pelvis, and when this portion of the abdominal cavity has been thoroughly washed out the lumbar regions are dealt with in a similar manner. After the irrigation has been completed, the patient is turned upon the face, so as to permit the escape of fluid by gravitation. A large glass drain is then inserted and its opening closed with salicylated cotton, after which the antiseptic dressing is applied in such a manner that the end of the tube remains accessible to the removal of fluid by aspiration as often as circumstances may require. In progressive sepsis, following in the course of progressive gangrene of a limb, amputation will become necessary if secondary disinfection and permanent irrigation have proved of no avail in arresting the septic infection. The general treatment of septic infection is the same as has been advised in cases of septic intoxication.

CHAPTER XIII.

PYÆMIA.

PYÆMIA, or pyohæmia, is a general disease caused by the entrance into the circulation of pus or some of its component parts, characterized by recurring chills, an intermittent form of fever, and the occurrence of metastatic abscesses. Although this disease was known a long time before Piorry applied to it the name it still bears, its intimate relationship to suppurative processes was first pointed out by this surgeon. Piorry maintained that, as the name implies, pyæmia is caused by the entrance of pus into the blood. Virchow, on the other hand, contended that no pus is found in the blood of pyæmic patients, and that the secondary or metastatic abscesses are not true abscesses resulting from the accumulation of pus derived from the blood, but that they are the result of embolic processes, puriform softening, inflammation, and suppuration around the blocked vessel. Recent bacteriological investigations have shown that Piorry's views are so far correct in that pus is produced within blood-vessels by the entrance of pus-microbes into the circulation. As a wound complication pyæmia can only occur after suppuration has taken place in a wound, and, as a complication of non-traumatic lesions, it can only develop in the course of suppurative affections. The great prevalence of pyæmia in overcrowded and badly-ventilated hospitals, during the time before the antiseptic treatment of wounds came into use, gave rise to a general belief that the disease was due to a specific cause, and ever since bacteriology became a science diligent search has been made to discover the specific microbe. Since the discovery of the microbes of suppuration, new light has been shed upon the etiology and pathology of this disease. Bacteriological examinations of pyæmic products have shown that one or more kinds of pus-microbes are always present, thus establishing the direct relationship which exists between a suppurating process in some part of the body and the development of metastatic or pyæmic abscesses. Clinical experience has only corroborated the scientific investigations of this subject, inasmuch as it has shown that the frequency of pyæmia has been diminished in proportion to the lesser frequency of suppurative inflammation under the antiseptic treatment of wounds and suppurating lesions. We are justified, upon the basis of well-established facts, in claiming that pyæmia is not a disease *per se*, but that its occurrence depends upon an extension of a suppurative process from the primary seat of infection, and suppuration in distant organs by the transportation of emboli infected with pus-microbes through the systemic circulation. The distant, or metastatic, abscesses contain the same microbes which are found in the wound-secretions, or in the abscess from which the general purulent infection took place. Experiments have shown that a culture of pus-microbes from a furuncle may produce pyæmia in animals, and that the microbes cultivated from a pyæmic abscess, when injected under the skin of an animal, may cause only a localized suppurative inflammation without any general symptoms.

BACTERIOLOGICAL AND EXPERIMENTAL RESEARCHES.

While the direct relationship existing between suppuration and pyæmia was well understood clinically for a long time, it was left for Klebs to demonstrate for the first time the direct connection of the pyæmic processes with the presence of specific microbes. In his researches into the nature of this disease during the Franco-Prussian war in 1870, he discovered in the pyæmic products certain micro-organisms which he called micrococci of pyæmia. He found that these microbes always arranged themselves in the form of colonies or groups which he termed *zoöglœa*. He found this microbe invariably present, notably at the primary seat of infection, but also in the most distant organs,—wherever, indeed, pathological changes occurred during the course of the disease. Pasteur, in studying the puerperal form of pyæmia, discovered a chain coccus which undoubtedly was identical with the streptococcus pyogenes, but which he called *microbe enchapelet.* Hueter and Vogt found a micro-organism in pyæmic products which they include among the monads. Burdon-Sanderson supposed that he had discovered the essential microbic cause of pyæmia in the shape of a "*dumb-bell shaped germ*," which in all probability was a staphylococcus.

Schüller examined the contents of metastatic joint affections in 12 cases of puerperal pyæmia, and invariably found pus-microbes. Rosenbach investigated 6 cases of typical pyæmia with a view to determine the nature of the microbes present in the pyæmic products. He found the streptococcus pyogenes present in the blood, and metastatic deposits in 5 of them; in 2 of these cases staphylococci were also present, although fewer in number. In only 1 of them he found staphylococci alone, and this case recovered. Pawlowsky made a bacteriological examination of the pus of metastatic abscesses in 5 cases of pyæmia. In 4 cases he found the staphylococcus pyogenes aureus, and in the fifth case, which was remarkable for the extent of the joint complications, he found the streptococcus pyogenes. He believes that the staphylococcus pyogenes aureus is the usual cause of pyæmia, and especially of that form characterized by multiple abscesses in the internal organs. Large cultures of this coccus suspended in water and injected subcutaneously in rabbits caused death, and at the necropsy multiple abscesses were found. He maintains that pyæmia in man occurs when disturbances in the circulation are present, so that floating cocci find favorable points for localization within the blood-vessels. He created such disturbances artificially in animals by making intra-venous injections of cinnabar, with the result that the glandular material determined localization of the microbes which were introduced into the circulation.

Besser examined bacteriologically blood, pus, and parenchymatous fluid from organs in 23 cases of pyæmia. In 8 cases the staphylococci albi and aurei were found; in 14, streptococci; and in 1, streptococci and staphylococci simultaneously. The microbes were discovered during the patient's life in pus in every one of 20 cases examined; in blood, in 11 of 12; and in parenchymatous serum, in 1. After death, in pus, in 17 of 17; in blood, 4 of 9; and in organs, 9 of 14. Besser's predecessors described 23 additional cases of pyæmia, in 14 of which staphylococci were found; in 7, streptococci. Total, 46 cases: in 22, staphylococci; in 21, streptococci; in 3, both. Besser was unable to detect the slightest morphological or pathogenic difference between the microbes of suppuration and those of pyæmia.

Okinschitz made the relationship which exists between the pus-microbes and pyæmia the subject of bacteriological investigation. He found that pyæmic blood invariably contained either the streptococcus pyogenes or the staphylococcus pyogenes aureus, demonstrated by cultivation and ordinary microscopical examination. As the hæmic microbes seldom show any signs of fission, as compared with the bacteria at the primary focus, it is reasonable to infer that reproduction takes place mainly in the pus, and not in the blood; hence the great importance of thorough disinfection and destruction of primary foci. The number of microbes in the circulating blood bears a direct relation to the gravity of the disease. If they are abundant, even in the absence of metastases in internal organs, the prognosis is grave, and if scanty, even if metastatic foci are present, the prospects of a favorable termination are better.

Pyæmia in Rabbits.—Koch produced pyæmia artificially in rabbits by injecting putrid fluids. A piece of a mouse's skin, about a square centimetre in size, was macerated for two days in 30 grammes of distilled water, and a syringeful of this fluid was injected subcutaneously into the back of a rabbit. Two days the animal remained apparently well, then it began to eat less, became gradually weaker, and died one hundred and five hours after the injection. An extensive subcutaneous abscess was found at the seat of injection. In the abdominal wall the yellowish infiltration extended in parts through the muscles and even to the peritoneum. The peritoneal surface presented evidences of inflammation. The intestines were adherent, and the peritoneal cavity contained a small quantity of turbid fluid. The liver showed on section gray, wedge-shaped patches. In the lungs infarcts the size of a pea were found. A syringeful of blood taken from the heart of this animal was now injected under the skin of the back of a second rabbit. The second animal died in forty hours, and at the necropsy nearly the same pathological conditions were found, only that the peritonitis was less advanced. Further experiments showed that $\frac{1}{10}$ drop of pyæmic blood proved fatal in rabbits in one hundred and twenty-five hours. All subsequent experiments proved that the less the quantity of blood injected the longer the time which elapsed before death occurred, but where the quantity was reduced to the one-thousandth part of a drop no result followed. On microscopic examination cocci were found in great numbers everywhere throughout the body, and more especially in the parts which had undergone alterations visible to the naked eye.

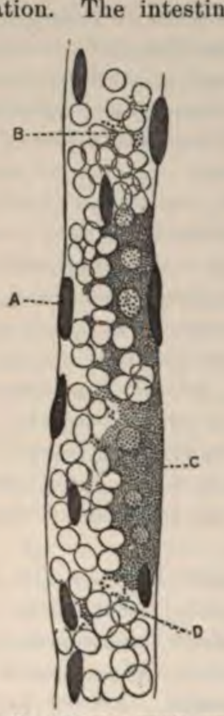

FIG. 78.—VESSEL FROM THE CORTEX OF THE KIDNEY OF A PYÆMIC RABBIT. × 700. (*Koch.*)*

A, nuclei of the vascular wall; B, small group of micrococci between blood-corpuscles; C, dense masses of micrococci adherent to the wall and inclosing blood-corpuscles; D, pairs of micrococci at the border of the large mass.

The description of the microbe found corresponds with the staphylococcus. The relation of the microbes to the blood-vessels could be seen best in the renal capillaries (Fig. 78). In the interior of the vessel, at C, is a dense deposit of micrococci adherent to the wall, and inclosing in its substance a number of red blood-corpuscles. The capillary stasis is either due to the power of the microbes of causing the red blood-corpuscles, to which they adhere, to stick together, or their property of producing in their immediate vicinity coagulation of the blood, and thus cause thrombosis. The microbes were found so arranged that they inclosed red blood-corpuscles in the capillary vessels of all the organs examined, as, for example, in the spleen and in the lungs. Koch believes that the large metastatic deposits in the liver and in the lungs do not arise by gradual growth of a mass of micrococci, as in Fig 78, but by the arrest of large groups and of the clots associated with them; in other words, by true embolism. In the metastatic deposits an extensive development of micrococci occurs, and these are not confined to the vessels, but invade the neighboring tissues. In the peritoneal cavity the micrococci were not found in large masses, but isolated, in pairs or in small groups.

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*Copied from "Traumatic Infective Diseases," by permission of the New Sydenham Society, London.

In the vicinity of the abscess he detected the microbes in the walls of veins, and their passage through these into the interior of the vessels could be readily discerned in many places. As Koch has pointed out, the microbe of pyæmia in rabbits, which is a pus-microbe, when brought in contact with the red blood-corpuscles, increases their viscosity and they form larger or small coagula in the blood. They can thus no longer pass through the minute capillary net-work, but are arrested in the smaller vessels. From the point of infection fresh micrococci pass constantly into the blood, and also individual micrococci will become detached from these small thrombi and emboli, and mix with the blood-stream. As the microbes are constantly being deposited by mural implantation, their number in the circulating blood always remains relatively small. Klein described a micrococcus of pyæmia in mice. Certain cocci which were present in pork proved fatal to mice in about a week, producing both purulent inflammation at the point of injection and metastatic abscesses in the lungs. Inoculations in the same species of animal with pyæmic products reproduced the disease in a typical manner. Pawlowsky found that by simultaneous injection of sterilized cinnabar, and of cultivation of staphylococcus pyogenes aureus into the circulation, he produced abscesses in various organs—in fact, the typical picture of pyæmia. The presence of particles of foreign bodies rendered material aid in the development of metastatic abscesses, as the mere arrest of pus-microbes in the circulation without them, as a rule, was not found sufficient of itself to lead to the production of true pyæmia. In rabbits, even, the introduction of a large quantity of a culture of pus-microbes into the circulation did not produce pyæmia. Twenty-four hours after the injection he found the microbes in large numbers in the pulmonary and other capillaries, but after forty-eight hours they had all disappeared from the blood. If the cocci are incorporated in, or are attached to, an embolus, this latter, by producing alterations in the endothelia of the blood-vessels at the point of impaction, create a *locus minoris resistentiæ* favorable to the growth of the microbes. In the experiments of Pawlowsky, the particles of cinnabar acted upon the endothelial lining of the capillary vessels in the same manner as the fragments of a thrombus, by impairing the local nutrition of the tissues with which they were brought in contact.

ETIOLOGY.

If pyæmia can be artificially produced in rabbits, mice, and guinea-pigs with pus, or with a pure cultivation of the same with or without the presence of foreign bodies, the same local conditions are first produced at the point of inoculation which invariably precede the development of pyæmia in man. Some of the veins at the seat of primary infection are invaded by pus-microbes, and become blocked by a thrombus; this thrombus undergoes puriform softening; small fragments containing pus-microbes become detached and are washed away and enter the general circulation as emboli, which, when they become arrested, establish independent centres of suppuration. In such cases the same microbes can be found in the wound, in the blood, in the tissues around the abscess, and in all distant pyæmic products. Although the streptococcus pyogenes has been found most frequently in the pus at the primary seat of infection and in the metastatic abscesses of pyæmic patients, there can be but little doubt that any of the pus-microbes, when present in sufficient quantity in the blood, can produce the disease. *The occurrence of pyæmia from suppurating wounds or abscesses does not depend so much upon the kind of pus-microbes which have caused the primary suppuration as upon surrounding circumstances. The location and anatomical structure of the tissues, in which the primary infection has taken place, exert an important influence in the production of the disease.*

It is an exceedingly familiar clinical fact that suppurative inflammation of the medullary tissue in bone is frequently the cause of pyæmia. Acute suppurative osteomyelitis, without direct infection through a wound, is always due to intra-vascular infection—localization of pus-microbes in the capillary vessels of the medullary tissue. The microbes come first in contact with the endothelial cells when mural implantation has taken place, and the coagulation necrosis which follows leads to thrombosis. The products of the intra-vascular coagulation necrosis furnish a most favorable nutrient substance for the growth and multiplication of the pus-microbes; consequently the area of intra-vascular infection is rapidly increased. The growth of the thrombus in a proximal direction soon leads to extensive thrombo-phlebitis, and, as softening of the thrombus takes place, to embolism and metastatic suppuration. Pyæmia following a suppurative inflammation in a wound, or in the course of a phlegmonous inflammation of the connective tissue, is the result of an infection with pus-microbes which penetrate the veins from without. The pus-microbes, coming first in contact with the outer coats of the veins, give rise to phlebitis, which progresses from without inward, and which is followed by thrombosis as soon as the intima is reached. The intra-vascular dissemination of the pus-microbes then takes place in the same manner as in cases of primary thrombo-phlebitis. *Ordinary pyogenic microbes may and do cause pyæmia, if they enter the blood incorporated in, or attached to, fragments of an infected blood-clot, or other solid materials, which, after they have become impacted in blood-vessels as emboli, prepare the soil in distant organs for their localization and reproduction.*

The importance of thrombosis and embolism, as essential factors in the causation of pyæmia, has been clearly established by clinical observation and experimental research. Emboli may originate in the lymphatic vessels when these are the seat of invasion by pyogenic microbes, which, however, is very seldom the case. In chronic pyæmia, in which multiple metastatic abscesses are formed, embolism takes no essential part in the process; the microbes enter the blood-current without such a vehicle, and are brought in direct contact by mural implantation with the interior lining of vessels weakened by injury, or other local and general debilitating influences. Experimental research has shown conclusively that the mere introduction of pus-microbes into the circulation is not necessarily, or even usually, followed by pyæmia, and their accidental entrance in the course of a suppurative inflammation is not always followed by serious consequences. *There can be no doubt that some pus-microbes reach the circulation in nearly every case of suppuration, but their pathogenic action is prevented, or neutralized, by an adequate resistance on the part of the tissues with which they are brought in contact and their rapid elimination through healthy excretory organs.* A limited number of pus-microbes injected into the circulation of a healthy animal, or accidentally introduced into the blood of an otherwise healthy person, are effectively disposed of by the white blood-corpuscles. If, however, the same number of microbes are present in combination with fragments of a blood-clot, the infected foreign particles produce such nutritive changes in the tissues surrounding them as to transform them into a favorable soil for the pathogenic action of the microbes. The same happens if free pus-microbes localize in a part the vitality of which has been previously diminished by trauma, or antecedent pathological changes, which constitute a *locus minoris resistentiæ* for the growth and multiplication of the pus-microbes. Pyæmia, therefore, must be looked upon rather as a serious and fatal complication of suppurative lesions than an independent specific disease. The immediate causes of pyæmia are the formation of an infected thrombus at the primary seat of infection and disintegration of this thrombus to such an extent that fragments become detached and are conveyed by the blood-current to distant organs, where they are arrested in the smaller arteries as emboli.

Thrombosis.—A thrombus is an intra-vascular blood-clot locally formed within the heart or a blood-vessel, and the process by which it is formed is called "thrombosis." A thrombus is called *venous* if it occur in a vein, *arterial* if it form in an artery. A red thrombus is produced if the blood coagulate in its entirety, while a white thrombus is composed of fibrin exclusively or the fibrin and the colorless and third corpuscles of the blood. A mural thrombus is a thrombus which is attached to the inner surface of a vessel-wall without occluding the entire lumen of the vessel. Notwithstanding the numerous and ingenious experiments which have been made for the purpose of ascertaining the immediate cause of intra-vascular coagulation of the blood, this subject awaits a more satisfactory explanation than can be given at the present time. Richardson, Bruecke, and Lister have shown that the mere mechanical interruption to the flow of blood in a vessel is not a sufficient cause of coagulation. Blood has been kept in a fluid condition in a vessel between two ligatures for an indefinite period of time in the living tissues.

Virchow, Cohnheim, Baumgarten, and Zahn maintain that the colorless corpuscles are in the closest manner related to thrombus formation. Zahn, from observations on the living mesentery of the frog, found that when the wall of a vessel was injured the colorless corpuscles accumulate around the injured part, constituting what he calls a white thrombus. The corpuscles subsequently, in great part, disintegrate and give rise to a granular accumulation, which, by its action upon the fibrinogen of the blood, causes a precipitation of fibrin.

Since the discovery of the third corpuscle, or *hæmatoblast*, by Hayem and Bizzozero, the part taken by this element of the blood in the process of coagulation has been carefully studied by Eberth and Schimmelbusch. The third corpuscle possesses a peculiar property to adhere to any foreign body or irregularity of surface of the intima of the blood-vessels. The authors just quoted found that when a vessel is injured, as by tying a ligature around it and removing this in a quarter of an hour afterward, these minute blood-disks manifest a peculiar tendency to adhere to the injured part of the tunica intima and to each other, forming a white mural thrombus. The process by which mural implantation of the third corpuscle takes place these authors call *conglutination*, the mass thus formed being composed primarily and exclusively of this morphological element of the blood. If an aseptic thread is drawn across the lumen of a vessel in which the blood-current is moving, the third corpuscle is arrested in its course and becomes deposited upon the thread, which in time becomes the centre of a white thrombus. Conglutination, under such circumstances, is a purely mechanical process.

Eberth and Schimmelbusch demonstrated by their experiments that conglutination is most liable to occur where irregularities of the tunica intima are present. If by a trauma inflammatory or degenerative changes take place, the endothelial lining of a blood-vessel is rendered rough and uneven; conglutination takes place first at the points which project farthest into the lumen of the vessel, because here the projecting body encroaches upon the axial current, which conveys the third corpuscle. In thrombosis from pathological causes, mural implantation of the third corpuscle takes place upon an intima roughened by inflammatory or degenerative changes. *Thrombus formation, as we observe it in pyæmia, always takes place upon a vessel-wall altered by the action of pus-microbes.* The form of thrombosis intimately associated with the etiology and pathological anatomy of pyæmia occurs in a vein within or in close proximity to the primary suppurative lesion. The close relationship of phlebitis to pyæmia was well understood by John Hunter, who believed that the former always preceded the latter. He taught that the phlebitis resulted in intra-venous production of pus and the formation of metastatic abscesses. Cruveilhier, on the other hand, regarded thrombosis as the first link in the chain of pathological conditions in pyæmia. The idea of primary thrombosis as a cause of disease was carried by his pupils so far that nearly all inflammatory processes were by them attributed to thrombotic changes in small veins; not only inflammatory lesions, but even tumors were supposed to originate in this manner. A new aspect was given to the pathology of this disease by the careful experimental investigations of Virchow on thrombosis and embolism. He showed that the metastatic deposits always occurred at points where vessels had been blocked by an embolus derived from a disintegrating thrombus. In the light of recent research phlebitis precedes thrombus formation at the primary seat of the infection. The pus-microbes which are present in the infected tissues permeate the vein-wall, and induce inflammatory changes characteristic of this form of infection. As soon as the infection has reached the intima this structure is roughened, and upon the projecting points conglutination takes place, and the foundation for thrombus is laid by a pavement composed of the third corpuscles of the blood. Upon this surface *aggregation* of the colorless corpuscles takes place, and, as these structures undergo coagulation necrosis, fibrin is formed and a mural thrombus is established.

The pus-microbes, which have reached the interior of the vein through the inflamed vein-wall, multiply in the thrombus, and produce here, as elsewhere under similar favorable circumstances, their specific pathogenic effect. The thrombus thus formed is an infected thrombus which precludes the possibility of its removal by absorption. With an increase of the intra-venous infection coagulation is hastened, and a red thrombus soon fills the entire lumen of the vein, surrounded by a zone composed exclusively of blood-disks, colorless corpuscles, and fibrin, which compose its mural portion. As soon as the lumen of the vein has been completely obstructed the conditions for coagulation are improved, and the thrombus increases in size in both directions. The contact of the blood with the dead, infected thrombus results in coagulation, and in this manner layer after layer is added to the thrombus. If thrombus formation take place in advance of the primary phlebitis, inflammation of the vein-wall follows as an inevitable consequence from the presence of the infected thrombus, the inflammatory process spreading like the infection from within outward. The growth of a thrombus is seldom arrested in a central direction until some large vein-trunk is reached, into which the apex of the thrombus projects.

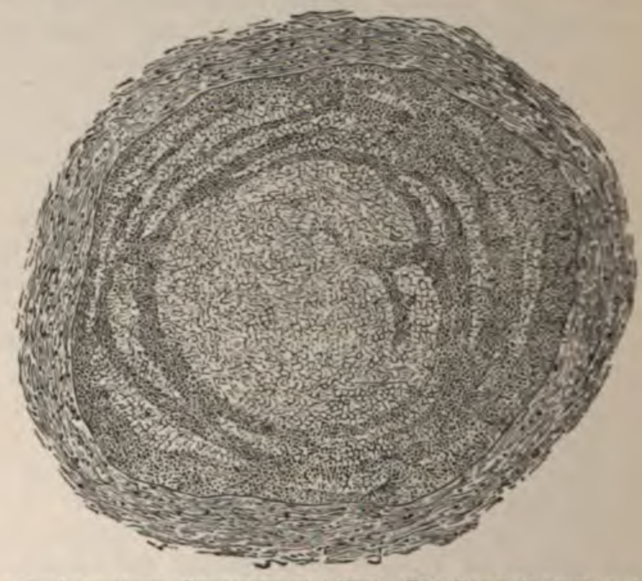

FIG. 79.—LAMINATED THROMBUS IN A VEIN. THE DARK GRANULAR LAYERS ARE COMPOSED OF COLORLESS BLOOD-CORPUSCLES AND FIBRIN; THE CENTRAL, LIGHTER PORTION, OF RED CORPUSCLES. 1:97. (*Birch-Hirschfeld.*)

The blood-current in a vein into which the apex of a thrombus from an adjacent vein projects frequently arrests its proximal extension, but if the venous circulation is impeded, or the thrombus continues to grow by the addition of new layers, in spite of the obstacles presented, one portion after another of a vein becomes involved, and the thrombus rapidly increases in length in a proximal direction. A venous thrombus in a pyæmic patient is only loosely attached to the vein-wall, as the pus-microbes transform the white corpuscles, which remain after coagulation has occurred, into pus-corpuscles, and in this manner softening and disintegration of the thrombus are accomplished. If a thrombus, at the point where it is in contact with the venous circulation on the proximal side, become sufficiently softened, fragments become detached and are carried away by the venous current as emboli.

Embolism.—*An embolus is a detached thrombus, part of a thrombus, or any foreign substance transported by the arterial blood-current to its place of impaction. The process or act by which this is accomplished is called embolism.* An aseptic embolus produces disturbances at the seat of impaction, which result exclusively from the sudden interruption of the blood-supply to the tissues fed by the obstructed vessel. The effect on the tissues is the same as though the vessel had been tied with an aseptic ligature. Virchow found that aseptic caoutchouc emboli, introduced into the right side of the circulation through the jugular vein, produced no serious trouble after their impaction in the branches of the pulmonary artery.

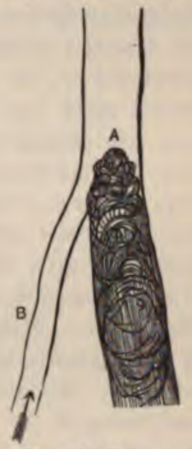

FIG. 80.—THROMBOPHLEBITIS. (*Billroth.*)

A, central end of venous thrombus projecting into a larger vein-trunk; B, vein-branch not closed by a thrombus.

Panum ascertained, by his experiments, that small, simple emboli in the pulmonary artery become encysted. The emboli of fœtal cartilage which Maas introduced into the jugular vein in dogs did no damage to the pulmonary tissue, and not only retained their vitality but became the nucleus of a temporary tumor. An aseptic embolus, derived from plastic intravascular exudations or an aseptic thrombus, affects the tissues at the seat of impaction in the same manner as the aseptic substances which have been used to produce embolism artificially in animals. *An embolus consisting of a fragment of an infected thrombus, as is the case in pyæmia, is a culture medium which contains the same microbes as caused the primary infection, and which at the seat of impaction establishes an independent centre of infection, which etiologically and pathologically is identical with the primary invasion.*

The embolic origin of metastatic abscesses was first pointed out by Virchow, who, at the same time, showed that the emboli are always derived from venous thrombi undergoing puriform softening. The closure of a vessel by thrombosis is always a slow, gradual process, while the obliteration of an artery by an embolus is the work of a moment. The gradual closure of a vessel by the slow growth of a thrombus is not attended by the same degree of disturbance of nutrition as when a vessel of similar size is suddenly blocked by the impaction of an embolus. Septic thrombo-phlebitis does not lead at once to embolism, as new layers are constantly being added to the proximal end of the thrombus, from where the fragments which constitute the emboli are always derived. Embolism only occurs if the proximal end of the thrombus has become sufficiently softened that fragments separate spontaneously and enter the venous circulation, or if the fragments are washed away by the venous current from a projecting thrombus. As the infected thrombus is always located in a vein within, or in close proximity to, the seat of primary infection, the detached fragments or emboli reach the right side of the heart with the venous blood, and, as they are usually too large to pass through the pulmonary capillaries, they become impacted in the branches of the pulmonary artery. *The lung acts as a filter, and is therefore the most frequent seat of embolism and metastatic abscesses.* The circulatory disturbances at the seat of impaction give rise to pathological conditions which are characteristic of embolism, and can be readily recognized in the examination of organs after death. *The area of tissue affected by the sudden closure of a vessel by the impaction of an embolus is called an infarct, and the process which produced the pathological changes infarction. Infarcts are always wedge-shaped, the apex of the triangle corresponding to the location of the embolus, and the base to the ultimate branches of the obliterated vessel.*

Cohnheim has described what he calls a terminal artery, by which is meant one whose branches inosculate only with those of the corresponding vein, one which is devoid of collateral anastomosis. Such are the renal and splenic arteries, and, in a less complete manner, those of the brain, heart, stomach, and lungs. If a terminal artery in the kidney or spleen is obstructed collateral circulation cannot be established, and necrosis of the tissues which depend on the closed artery for their blood-supply is an inevitable consequence. The same result follows embolism of a terminal artery in the spleen. In the other organs which have been enumerated the terminal arrangement of the arteries is not as absolute, and embolism is not followed by necrosis with the same degree of certainty, as circulation cannot be restored, under favorable circumstances, by collateral branches. The first effect of the closure of an artery, by an embolus in any of these organs, is the appearance of a wedge-shaped area of ischæmia, which in size corresponds to the size of the vessel obstructed. It may be so small that it can hardly be detected by the naked eye, or the base of the wedge may be 1½ inches in length. The border of this wedge-shaped space becomes the seat of active hyperæmia, the surrounding vessels undergoing rapid dilatation. The hyperæmia is usually so intense that rhexis takes place and the parts become infiltrated with blood; hence the expression *hæmorrhagic infarct.*

Hamilton is of the opinion that the hæmorrhagic infarcts in the lung are not caused by embolism, but by rupture of small vessels and hæmorrhage into the alveoli, the distribution of the fine branches of the bronchi determining the shape of the infarct. Although the ultimate branches of the pulmonary artery cannot be called terminal arteries, in the strictest sense implied by this term, if they become suddenly blocked by an embolus, collateral hyperæmia is so intense that hæmorrhage into the parenchyma of the organ frequently takes place,—a condition well represented in Fig. 81.

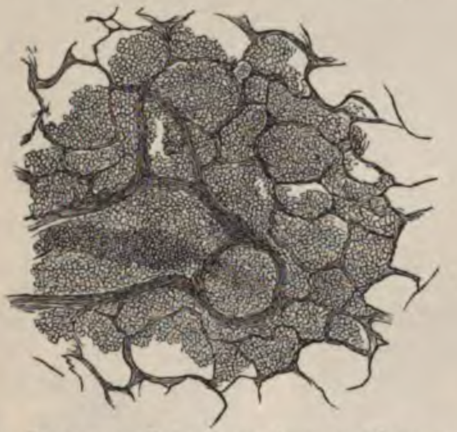

FIG. 81.—EMBOLUS OF BRANCH OF PULMONARY ARTERY. HÆMORRHAGIC INFARCTION OF ALVEOLI. CHROMIC-ACID SPECIMEN. 1:100. (*Birch-Hirschfeld.*)

In hæmorrhagic infarcts of the lung resulting from embolism the tissues involved are firmer than normal, and, on section, present pneumatic appearances, which are due to infiltration with leucocytes and extravasation of blood, as well as transudation of blood-plasma through the walls of the hyperæmic blood-vessels surrounding the ischæmic area. As the emboli usually lodge in the peripheral branches of the pulmonary artery, the infarcts are most frequently located near the surface of the lung. Immediately after embolism has occurred the district supplied by the obstructed vessel presents an anæmic appearance, which soon gives place to a reddish color, resulting from the hæmorrhagic infiltration. As in pyæmia the embolus conveys from the primary seat of infection the specific microbes of suppuration, it becomes the centre of a suppurative inflammation. The pus-microbes multiply in their new location and at once induce a suppurative arteritis, and, after their passage through the inflamed vessel-wall, they attack the histological elements contained in the exudation, which breaks down, becomes purulent, and is converted into an abscess. In the lung the leucocytes which are present in the infarct are converted into pus-corpuscles, and the interstitial connective tissue undergoes necrosis and can be found as detached shreds in the abscess.

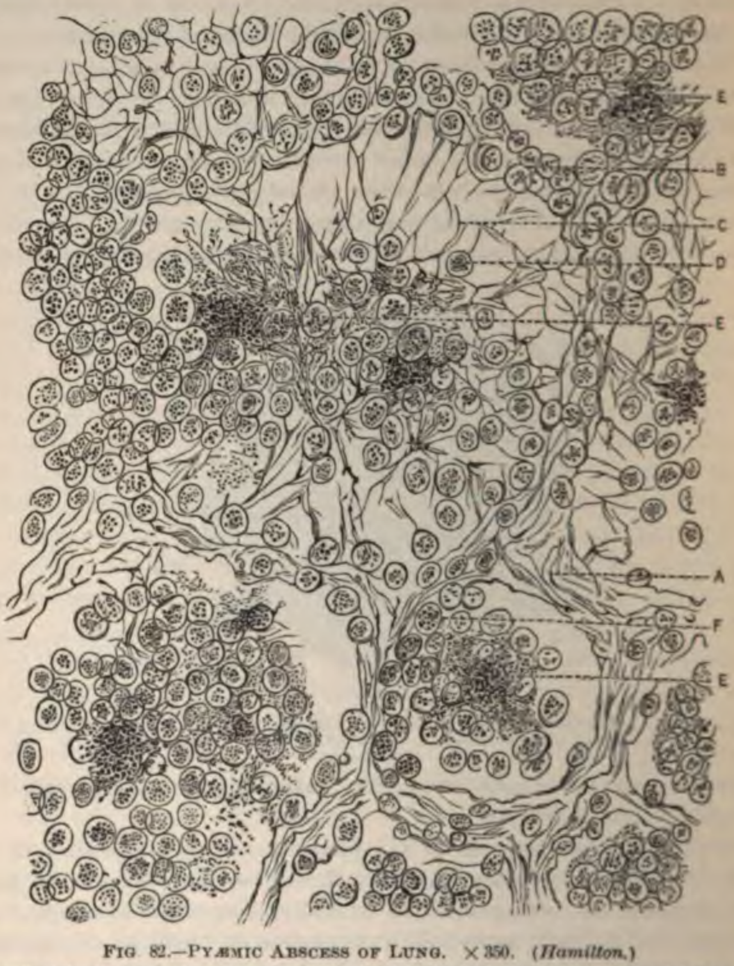

FIG. 82.—PYÆMIC ABSCESS OF LUNG. × 350. (*Hamilton.*)

A, walls of alveoli; B, effused, small, round cells; C, fibrin lying in alveolar spaces; D, cell entangled in meshes of same; E, E, E, masses of micrococcus (staphylococcus) lying in exudation.

Embolism and metastatic abscesses, although more frequently found in the lungs in pyæmia, are not limited to this organ. To explain the occurrence of embolism in more remote organs, as the kidneys, spleen, liver, brain, etc., we must assume either that an embolus in the pulmonary artery becomes the nucleus of a thrombus, which, by its growth, reaches across the pulmonary capillaries and projects into the pulmonary vein, where fragments again become detached and enter the systemic circulation, or zoöglœa of pus-microbes, passing the first filter (the lungs), are arrested in the capillaries of distant organs, or, finally, leucocytes impregnated with pus-microbes serve as minute emboli, and, after their localization in distant organs, become the cause of metastatic suppuration. In the kidney the infarctions appear as sharply circumscribed areas of a pale, cream-yellow color. When cut into, the infarct has a wedge shape, the narrow end pointing to the hilus. The red zone is not so marked as in infarctions of the spleen, and the greatest vascularity is in the direction of the embolus. As in infarcts of the lung, the hyperæmic zone corresponds to the vessels nearest the ischæmic area. Extravasation of blood, although present, is never so marked as in the lung. The epithelial cells within the hyperæmic zone are destroyed by coagulation necrosis, and if the embolus is aseptic this portion of the kidney is removed by molecular degeneration and absorption, leaving a cicatrix behind.

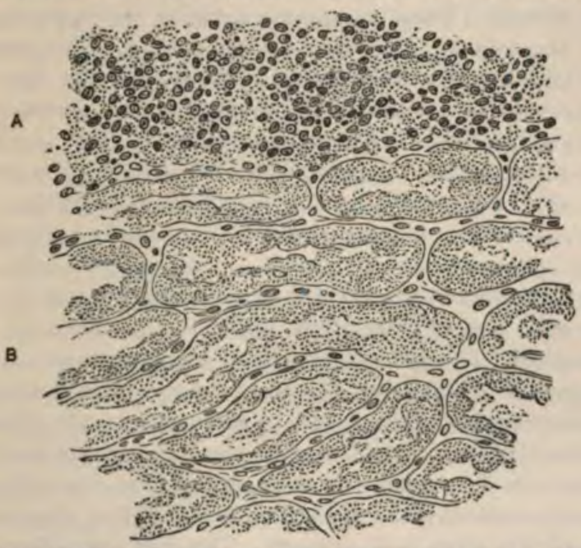

FIG. 83.—COAGULATION NECROSIS FROM A KIDNEY INFARCT. × 300. (*Birch-Hirschfeld.*) A, zone of reactive inflammation; B, loss of nuclei in the necrosed epithelia. (The nuclei of connective-tissue cells are in part preserved.)

Infarcts of the kidney occurring in pyæmia are converted into abscesses in the same manner as in the lungs, by the escape of pus-microbes from the embolus through the inflamed arterial wall into the tissues starved by defective blood-supply.

SYMPTOMS AND DIAGNOSIS.

As a wound complication pyæmia never occurs before suppuration has taken place, seldom before the seventh, usually about the ninth to eleventh, day after the accident or operation, if it is the result of a primary infection of the wound. In patients threatened with pyæmia, an ill-defined train of premonitory symptoms precede the actual development of the disease These symptoms apply to the appearance of the wound and the general condition of the patient. The onset of the disease may be suspected at any time after suppuration has occurred, when evidences of serious capillary stasis manifest themselves at the seat of injury or operation. The thrombo-phlebitis gives rise to œdema; the margins of the wound appear puffed and elevated, the granulations pale and flabby; suppuration, which may have been profuse, becomes scanty; the pus changes its character, and, instead of a yellowish, cream-colored fluid, it becomes sanious, serous, or sero-sanguinolent.

Careful inspection of the parts at this time may reveal the existence of thrombosis in one or more of the veins leading from the focus of primary infection. The general premonitory symptoms are indicated by a slight degree of intoxication, the result of the introduction into the circulation of pus-microbes and their ptomaines, from the primary focus of suppuration, causing a slight rise in the temperature and a general feeling of malaise, thirst, and loss of appetite. The actual development of the disease is initiated by a well-marked severe chill or rigor, which lasts from a few minutes to an hour or more. The chill resembles a malarial chill, and has often been mistaken and treated as such. Such a chill in a patient suffering from a suppurating wound or abscess is always an alarming symptom. It is an entirely subjective symptom, as the thermometer placed in the axilla during the algid stage indicates a rise in the temperature, which often reaches 104° to 105° F. before the patient ceases shivering.

Chills have been artificially produced in animals by the introduction of foreign substances into the circulation, and in pyæmia it is an indication that fragments of an infected thrombus, and with them a large quantity of pus-microbes, have entered the circulation. The chill may recur at regular intervals daily or every other day,—a feature which may still further add to the difficulty in making a differential diagnosis between pyæmia and malaria. Usually, however, the chill recurs at irregular intervals, one, two, or three times a day, as a rule, increasing in frequency, and often in intensity, as the disease progresses. If, for instance, during the first few days the patient has one chill daily, and, after a few days two or more during the same time, every additional chill indicates a more advanced stage of intoxication, and an increase in the number of metastatic foci. After the chill the fever continues for several hours, with a temperature of 103° to 104° F., until the appearance of profuse perspiration, when the temperature falls to normal, or even a little below that. The chill, fever, and sweating coming in the same order and of about the same duration as in malaria, the clinical picture resembles the latter almost to perfection, and on this account many cases of pyæmia have been mistaken in the beginning for malaria, and *vice versâ*.

The fever which attends pyæmia always is of an intermittent or remittent type. In acute pyæmia the chills may return several times during twenty-four hours, the temperature between them showing remissions, but seldom returning to normal. In subacute and chronic cases the remissions are well marked between the chills, the temperature often sinking below normal. Vomiting and diarrhœa are less constant symptoms than in septicæmia. The pulse in its frequency corresponds to the temperature; its force is always reduced by the depressing effect of the ptomaines upon the heart. Delirium is occasionally present, but, as a rule, the mind is clear until the end. The yellowish color of the skin, almost constantly present in pyæmia, has been attributed to icterus, resulting from metastatic processes in the liver; but in the majority of cases it is not the result of retention and absorption of bile, but is caused by destruction of red blood-corpuscles and pigmentation of the tissues with the coloring material thus liberated. It is an icterus, which, on account of its origin, is called "*hæmatogenous icterus*" The metastatic deposits in the kidneys are indicated by the appearance of albumen and sometimes pus in the urine.

Metastatic Suppuration.—Infarcts in one or more of the internal organs are present in every case of pyæmia, and suppuration in some of the large cavities is of frequent occurrence. In reference to the number of secondary metastatic foci of suppuration, a great deal depends on the clinical form which the disease assumes. In the acute form, which proves fatal within one to three weeks, the infarcts are numerous and the abscesses quite small, while in some of the infarcts the existence of suppuration cannot be demonstrated macroscopically. In chronic pyæmia, in which life is prolonged for months, and sometimes even a year, the number of secondary foci are few, but they have resulted in the formation of large abscesses. The presence of infarcts of the lung are indicated by symptoms and signs which point to circumscribed foci of inflammation in this organ. If the infarct is immediately underneath the pleura, it gives rise to circumscribed pleuritis and sharp, lancinating pain at a point corresponding to the location of the infarct, always aggravated by the respiratory movements. In such cases friction-sounds can often be heard over the infarct. The consolidation of the tissues involved by the infarct by inflammatory infiltration from the vessels surrounding it is attended by crepitant râles, bronchial breathing, and dullness on percussion, over an area corresponding to the size of the infarct. A pulmonary abscess which takes the place of an infarct increases in size by encroaching upon the surrounding tissues, and in chronic cases may empty itself into a bronchial tube. A subpleural infarct, infected with pus-microbes, not infrequently leads to suppurative pleuritis and empyema by the extension of the infection from the lung-tissues to the adjacent pleura. In the same manner a suppurating infarct of the lung may become a direct cause of suppurative pericarditis, and pyocardium if its location is adjacent to the pericardium. The onset of metastatic foci in the lungs is often insidious, and even large infarcts often occasion only slight subjective symptoms and objective signs. Embarrassed breathing should admonish the attendant to search for evidences of multiple infarcts of the lung. Abscesses in the liver, caused by septic emboli, vary in size from that of a pea to an orange, but occasion no symptoms unless they are located immediately underneath the serous covering, when they cause localized pain. Embolic infarcts in the kidneys may be suspected if the urine contains albumen, or pus, or both. The spleen is always enlarged in pyæmia, but, as this is the case in all acute infective processes, the presence of an infarct or abscess is only to be suspected if the symptoms, especially pain and circumscribed tenderness, point to the existence of perisplenitis. Enormous pyæmic abscesses often develop insidiously and without pain, or the ordinary symptoms of acute inflammation between muscles and in the subcutaneous connective tissue. Metastatic suppuration in pyæmia takes place not only where infarction has occurred, but also in localities where the existence of embolism cannot be demonstrated anatomically, this being notably the case in joints and the large serous cavities. Suppurative pericarditis, pleuritis, and peritonitis frequently complicate acute, rapidly-fatal pyæmia. Suppurative synovitis, multiple or limited to one joint, is a frequent complication, both in acute and chronic pyæmia. Metastatic suppuration in these localities develops without demonstrable infarcts, and occurs, in all probability, in consequence of mural implantation of pus-microbes or infected leucocytes upon the wall of capillary vessels, the intima of which has been damaged by ptomaines held in solution by the circulating blood. As in all cases of pyæmia pus-microbes and their ptomaines necessarily constantly enter the circulation from the primary focus of infection, they prepare the soil for the reception and pathogenic action of pus-microbes in the vessels and tissues of certain organs, more especially the synovial membrane of joints and the serous membranes lining the large cavities. Pyæmic abscesses, when well-developed, always contain yellow pus of the consistence of cream. Examined under the microscope, such pus contains corpuscles in which no sign of a nucleus can be found.

The pus-microbes are always present in great numbers, both within the pus-corpuscles and in the pus-serum. While some doubt may remain after the first chill as to the nature of the disease, this doubt is dispelled with the recurrence of the chills. In acute cases the chill returns once or twice daily, but, unlike in cases of malaria, if the chill is of daily occurrence, it does not come at a fixed time, as is the case in malaria. If the disease does not culminate into a daily chill, the temperature then shows an irregular remittent type of fever. The patient loses strength and flesh rapidly, and the face presents the color of a mixture of the hectic flush with the icteric hue. While the pulse at first rises only to 100 to 120 beats per minute during the febrile exacerbations, it soon remains at from 120 to 150 per minute. Great thirst and complete loss of appetite remain constant symptoms. The tongue and lips are dry, diarrhœa is more common as septic intoxication advances, and the stools are frequently stained with blood. As the fatal termination approaches, delirium and sopor come on, and under increasing symptoms of depression death takes place gradually from heart-failure, or suddenly from embolism of the pulmonary artery. In chronic cases the duration of the disease is sometimes prolonged for months, and Billroth relates a case where the patient lived for a year. In chronic cases the chills recur at long intervals, and the fever assumes a remittent type between them. In still another class of chronic pyæmia the chills ultimately disappear, and the fever assumes a mild, continuous type, while the patient gradually succumbs to decubitus, amyloid degeneration of internal organs, or a slow form of septic intoxication.

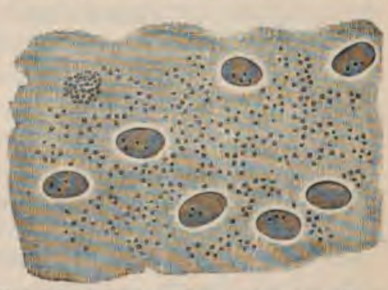

FIG. 84.—PYÆMIC PUS, SHOWING COMPLETE NUCLEAR DESTRUCTION IN CORPUSCLES AND AN ABUNDANCE OF PUS-MICROBES WITHIN AND BETWEEN PUS-CORPUSCLES. (*Landerer.*)

PROGNOSIS.

The prognosis of pyæmia is always grave. Acute pyæmia, in spite of all treatment, almost without exception terminates in death in from one to two weeks. The few recoveries which have been reported were cases of subacute or chronic pyæmia. As pyæmia is not a primary, but secondary, condition, it is a fatal disease from the very beginning, as during its commencement transportation of infected tissue has taken place to localities inaccessible to radical treatment. In acute cases death seldom takes place before the end of the first week, more frequently from the second to the end of the third week. In chronic cases not complicated by pulmonary infarcts, the metastatic suppuration in parts accessible to surgical treatment are occasionally amenable to successful treatment, and a cure can be obtained after a long and lingering illness. Prospects of a successful issue in chronic cases can be only entertained when the disease attacks young individuals otherwise in good health. The prognosis of pyæmia is also modified by the location of the primary focus of infection, as when this is not accessible to direct treatment the disease will progress uninfluenced by general treatment. If, on the other hand, further supply of septic material from the primary infection-atrium can be prevented by a prompt removal of the infected tissues, one of the most important indications of treatment has been met, and the hope of a favorable termination has been thereby increased.

PATHOLOGICAL ANATOMY.

The pathological changes found in patients who have died of pyæmia are characteristic. The primary focus of infection may no longer be present, as it may have healed, but, as a rule, this has not occurred, and examination shows a suppurating wound, an abscess, an osteomyelitic focus, a suppurating phlebitis or sinus phlebitis. The vein in which the fatal thrombus formed may not be a large one; indeed, it may be so small as to elude detection by macroscopical examination. If the immediate cause of the pyæmia, the thrombosed vein, can be located, it will be found filled with a softened, loose blood-clot, which is very variable in length, and the proximal end of which projects usually into the lumen of some larger vein-trunk on the proximal side. The vein-wall itself is in a state of suppurative inflammation that prevents the formation of firm adhesions between the thrombus and the intima, as we find it in cases of *plastic* thrombo-phlebitis. The new histological elements that are produced by the inflammatory process are at once converted into pus-corpuscles, and some of these are distributed through the substance of the blood-clot, and furnish an additional cause for the softening and disintegration of the coagulum. The infarcts are most numerous in the lungs, but are also found in the spleen, kidneys, and liver. An embolus catches in an artery at a point where the lumen suddenly becomes smaller, which is the case where the vessel bifurcates. The embolus, after it has become impacted, becomes the nucleus of a thrombus, as the blood which comes in contact with it undergoes coagulation, and in this manner layer after layer are added on each side. As the embolus under these circumstances is always composed of dead infected material, it causes at the seat of impaction a specific inflammation, which in every respect represents the type of inflammation at the primary seat of infection. *As the tissues which are in immediate contact with the embolus are the coats of an artery, a suppurative arteritis* follows the impaction, and as soon as the pus-microbes have passed through the softened, inflamed arterial wall the infection extends to the tissues weakened by the sudden abstraction of blood; that is, the tissues which are within the borders of the wedge-shaped infarct. The hyperæmic zone around the infarct constitutes a wall of protection against unlimited extension of the infection and inflammation. In the lungs the infarct becomes rapidly infiltrated with the products of inflammation from the hyperæmic zone, which gives rise to consolidation of that portion of the lung. Suppuration is attended by liquefaction of the exudation, and the infarct is transformed into an abscess.

In pyæmia the emboli that reach the systemic circulation are smaller than those which reach the pulmonary artery; consequently the infarcts, as a rule, in the kidney, spleen, liver, and other distant organs are smaller than those in the lungs. In metastatic suppuration without embolism, in the strict sense in which this word has been heretofore used, the pus-microbes which become implanted upon capillary walls, changed by the action of pre-existing ptomaines diffused in the blood, reach and infect the para-vascular tissues and the interior of large cavities, thus causing a rapidly-spreading, diffuse, suppurative inflammation. In metastatic suppurative inflammation of the cynovial membrane of joints, the peritoneum, pleura, and pericardium, the process represents all the essential features of a specific surface inflammation, characterized by rapid extension of the inflammation over the whole surface, and the accumulation of a large purulent collection in a short time. Microscopic examination of nearly all organs in fatal cases of pyæmia reveals the existence of coagulation necrosis resulting from the action of pus-microbes and their ptomaines upon tissues with which they have been brought in direct contact. The spleen is always enlarged and softened, even if no infarcts are present. The heart is flabby and the muscular tissue softened. The intestinal mucous membrane is swollen, vascular, softened, and at points shows submucous extravasation from rupture of capillary vessels,—

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As in these cases the metastatic suppuration, as a rule, is not caused by embolic infarcts, life is threatened by the secondary lesions, from which ptomaine intoxication is maintained, and from which new places may become infected by localization of pus-microbes in capillary vessels weakened by the action of ptomaines. Suppurating joints are incised, drained, and irrigated under strict antiseptic precautions, and if the metastatic suppuration is limited to a single joint this can be done with a fair prospect of a favorable result. Purulent collections in the serous cavities or connective tissue are dealt with in a similar manner. Careful attention to diet and the sanitary surroundings of the patient, combined with energetic surgical treatment of the suppurating foci, will, at least occasionally, be rewarded by an ultimate recovery.

SEPTICO-PYÆMIA.

In the absence of more accurate knowledge concerning the microbic cause of septicæmia, we must, at least for the present, assign to septicæmia and pyæmia the same bacteriological cause. That pus-microbes can produce septicæmia, when introduced into the circulation in sufficient quantity, has already been shown, and that pus-microbes have been frequently cultivated from septic products is a matter of demonstration; hence the disease, if not identical with pyæmia, from a bacteriological stand-point, is at any rate closely allied to it. It has also been shown that, in case the life of septic patients is prolonged for a sufficient length of time, the metastatic foci of inflammation are the seat of incipient suppuration; hence such cases resemble pyæmia upon a pathological basis. In pyæmia, after cessation of the rigors, which are the most characteristic clinical symptom of this disease, the fever resembles septicæmia, and, as the clinical picture thus developed rests upon pathological conditions typical of pyæmia, it would be proper to apply to such cases the term *septico-pyæmia*. For the same etiological and pathological reasons we apply the same term to septicæmia in which post-mortem examination reveals the presence of minute, multiple, suppurating foci.

Septico-pyæmia may be defined as a condition in which the symptoms indicate the presence of both septicæmia and pyæmia, and in which the post-mortem appearances point to septic and purulent infection. Leube described such a combination of the two diseases, which as yet are considered as distinct, occurring in patients in whom he was unable to trace the source of infection from without; hence he called the affection *spontaneous septico-pyæmia.* Litten, on the other hand, in similar cases, was always able to locate the infection-atrium, but the primary infection at the time acute symptoms set in had either disappeared or its location could only be ascertained by most careful examination. Jürgensen applied to these cases the lengthy compound word "*kryptogenetic-septico-pyæmia*," as he was unable to find a tangible infection-atrium. In a recent article on the subject he gives an account of 100 cases that came under his own personal observation. The patients were usually attacked first with acute pharyngitis, and, as this stage was generally attended by a chill and a general feeling of malaise, the patients generally attributed the onset of the disease to exposure to cold. In most cases the general infection was announced by a severe chill. Rapid loss of strength was one of the most prominent symptoms; the patients in a few hours after the chill became utterly prostrated. The symptoms which pointed to local processes during life were referred most frequently to the lungs, liver, spleen, pleura, heart, and the long bones. Whether the primary infection occurred through the pharynx, where the first symptoms were manifested, could not be definitely ascertained. In the acute cases, the symptoms were grave from the beginning and increased in intensity as the infection progressed, while, in the chronic cases, infection is kept up from some suppurating focus, and the disease may continue for several years. Subcutaneous and retinal hæmorrhagic extravasations were frequently observed. Post-mortem examinations revealed suppuration in some of the internal organs, and vascular changes which are characteristic of sepsis.

These cases may be compared with acute suppurative osteomyelitis, where, after the most careful inquiry and the most scrutinizing examination, we often fail in furnishing reliable evidence for locating the primary source of infection. It is possible that the pus-microbes enter through an intact or inflamed mucous membrane, or through the appendages of the skin, and that they remain in a latent, inactive condition until a weak point is created somewhere in the body, where they localize in a soil prepared for their reproduction and pathogenic action, or, what is more likely the case, they entered through an abrasion or slight lesion, which may have been so insignificant that the patient himself failed to notice it, and produced no symptoms until, by accident or disease, a proper soil was prepared for the initiation of an acute attack in one or more of the internal organs. The remote dangers which may follow infection through an insignificant wound, or from a small, suppurating focus, should remind the surgeon of the importance of treating these little ailments with the necessary care and attention, and by so doing he will often be the means of preventing fatal complications. In 2 cases of kryptogenetic septico-pyæmia that have come under my own observation the disease was complicated by ulcerative endocarditis. In 1 of these cases the immediate cause of death was gangrene from embolism of the popliteal artery.

CHAPTER XIV.

ERYSIPELAS.

ERYSIPELAS is a self-limited, acute, non-suppurative inflammation of the lymphatic vessels of the skin or mucous membrane, attended by redness and a continued type of fever. As a wound complication it occurs independently of suppuration, and in its uncomplicated pure form remains as a superficial affection, the inflammation never passing beyond the structures of the skin or mucous membrane.

HISTORY OF ITS MICROBIC ORIGIN.

The contagiousness of erysipelas has been recognized for centuries, and on this account early attempts were made to include it among microbic diseases. In 1868 Hueter maintained that erysipelas and hospital gangrene were identical diseases and caused by the same micro-organism. Its microbic nature was again made the subject of investigation in 1872, when Napveau discovered micrococci in the blood of erysipelatous patients. Wilde detected the same microbes in the blood, but asserted that similar micro-organisms could be found in the pus in wounds from which the erysipelas developed.

In 1874 Recklinghausen found masses of micrococci in the lymphatic channels in the inflamed skin at the border of an erysipelatous inflammation. Nearly the same time similar observations were made by Billroth, Ehrlich, Tillmanns, and Koch. Tillmanns produced the disease artificially in animals by injecting subcutaneously the serum contained in the bullæ of erysipelatous skin.

Koch attempted to produce the disease artificially in rabbits with injections of different putrid fluids, but failed until he made inoculations with mouse-dung softened in distilled water. He injected the material under the skin of the ear, and produced an inflammation which in its course resembled erysipelas. The swelling and redness spread slowly downward from the point of inoculation. On the fifth day it had extended as far as the root of the ear. The ear became exceedingly vascular, so that the separate vessels could no longer be identified, while the tissues were softened and œdematous. The animal died on the seventh day. Blood taken from the heart of this animal produced no effect in other rabbits. No microbes could be found in the blood or in any other organ except the affected ear. In transverse sections of the ear the blood-vessels were seen to be markedly dilated, full of red corpuscles, and surrounded by the nuclei of white corpuscles. Between these and the cartilage-cells bacilli were found.

The bacilli were present close to the cartilage only. Here they were found in large clusters, from which the bacilli radiate in all directions. This net-work of bacilli extended over the whole cartilage of the ear on both surfaces. Inflammation was most marked in the vicinity of the bacilli, and, consequently, in the absence of other causes, there could be no doubt that the erysipelatous inflammation was caused by these

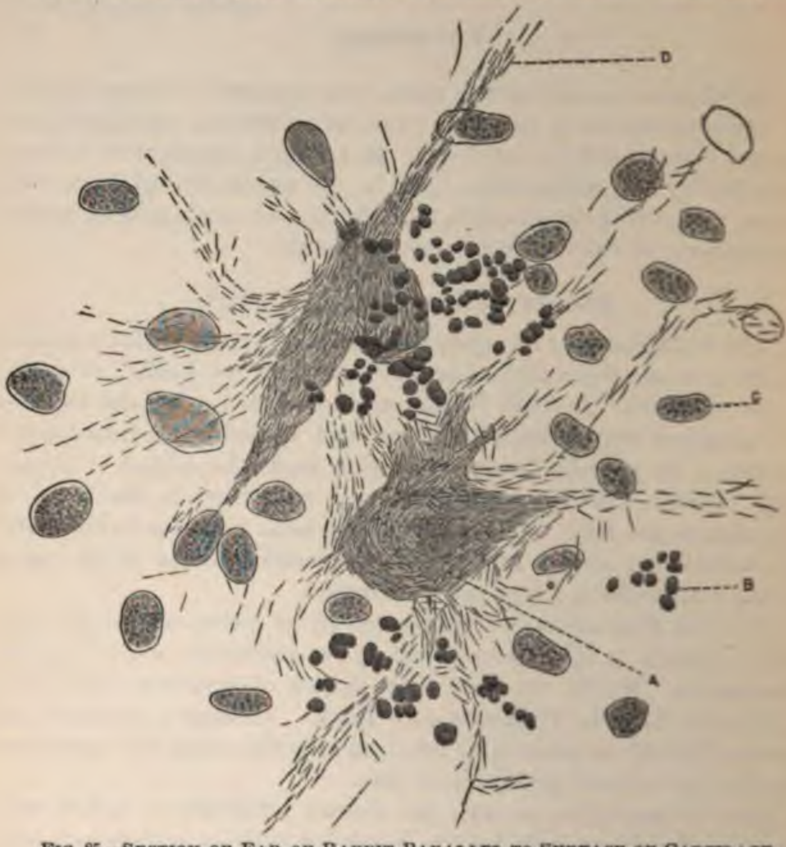

Fig. 85.—Section of Ear of Rabbit Parallel to Surface of Cartilage. The Morbid Process Resembled Erysipelas. × 700. (*Koch.*)*

A, ball-like accumulation of bacilli; B, accumulation of nuclei above the layer of bacilli; C, nuclei of flat cells connected with the cartilage below the layer of bacilli; D, bacilli arranged parallel to each other.

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* Copied from "Traumatic Infective Diseases," by permission of the New Sydenham Society, London.

microbes. Orth found micrococci in the contents of the bullæ of erysipelas. Recklinghausen and Lukowsky found them in the lymphatic vessels and the connective-tissue spaces in the structures affected by erysipelas. Billroth and Ehrlich found bacteria not only in the lymphatic vessels, but also in the blood-vessels of the inflamed skin. Tillmanns found microbes in erysipelatous skin, and Letzerich, in cases of erysipelas attacking vaccination wounds, found them in the wound itself, in the blood-vessels, muscles, liver, spleen, and kidneys. The essential specific cause of erysipelas was finally discovered by Fehleisen in 1883. He cultivated the microbe from erysipelatous products, and demonstrated its essential etiological relationship to erysipelas by producing the disease artificially, in animals and man, by inoculations with pure cultures. From the morphological appearance of the microbe and its direct etiological bearing to erysipelas he called it the *streptococcus of erysipelas.* With pure cultures of this microbe he produced by inoculations not only erysipelas in animals, to prove its specific pathogenic qualities, but successful inoculations were also made in man for therapeutic purposes.

DESCRIPTION OF STREPTOCOCCUS ERYSIPELATOSUS.

The streptococcus erysipelatosus, discovered by Fehleisen, when examined under the microscope appears in the form of chains, the links of which are minute cocci, 3 to 4 micromillimetres in diameter.

The streptococcus of erysipelas invades the superficial lymphatic channels of the skin or mucous membrane exclusively, but it can also be found in the serum contained in bullæ. Each coccus, when it is about to divide, becomes larger and oval, and soon appears made up of two hemispherical masses, the two new cocci resulting from fission of the old one. Morphologically, the streptococcus of erysipelas and the streptococcus pyogenes are nearly identical, only that the cocci of erysipelas are somewhat larger, while both are somewhat smaller than the staphylococci.

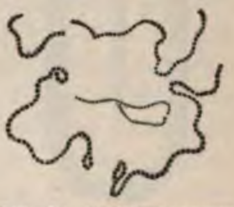

FIG. 86.—STREPTOCOCCUS ERYSIPELATOSUS. PURE CULTURE IN BOUILLON AT 37° C., STAINED WITH FUCHSIN. × 950. (*Baumgarten.*)

CULTIVATION.

This microbe can be readily cultivated in bouillon at ordinary room-temperature; also upon gelatin, agar-agar, and solidified blood-serum. Upon solid nutrient media the appearances of the cultures resemble very strongly those of streptococcus pyogenes. There is less tendency, however, to the formation of terraces the margin is thicker and more irregular in outline, and the appearance of the growth is more opaque and whiter. Rosenbach mentions, as another distinguishing feature between the two, that the culture of the streptococcus of erysipelas represents the shape of a fern, while the outlines of the cultures of the pus-streptococcus describe the shape of an acacia-leaf. The culture appears as a very delicate grayish-white film. The growth is very slow, and the individual colonies remain small. The streptococcus of erysipelas does not liquefy gelatin. The microbe of erysipelas grows equally well when oxygen is excluded. If gelatin is inoculated by puncturing with a needle charged with a pure culture, microscopical colonies can be seen the whole length of the track of the needle at the end of twenty-four hours. In four days the culture has reached the height of development, and colonies the size of a grain of sand to that of a pin's head occupy the whole length of the needle-track.

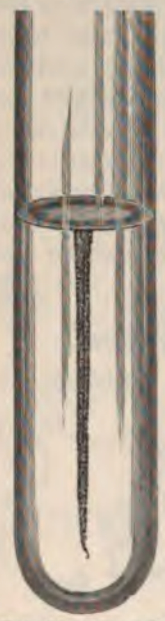

FIG. 87.—STALE CULTURE OF STREPTOCOCCUS OF ERYSIPELAS IN GELATIN AT ORDINARY TEMPERATURE OF ROOM, FOUR DAYS OLD, NATURAL SIZE. (*Baumgarten.*)

In cultures the microbe retains its pathogenic qualities for about four months.

INOCULATION EXPERIMENTS.

Fehleisen produced, artificially, typical erysipelas in rabbits by injecting pure cultures under the skin of the ear. Koch and Gaffky used cultures grown upon solidified blood-serum and inoculated 9 rabbits. In 8 of these typical erysipelas developed, the attack lasting from six to twelve days.

Krause obtained positive results by inoculating gray mice. In all cases where the inoculation proved successful the erysipelatous inflammation started at the point of inoculation, and extended rapidly, always following the lymphatic channels. In Krause's experiments the animals died after three or four days, even when only a minute quantity of the culture was injected under the skin of the back. Examination of the infected tissues after death showed that inflammation followed the invasion of the microbes, and consequently the principal pathological changes were found within and in the immediate vicinity of the lymphatic channels.

INOCULATION FOR THERAPEUTIC PURPOSES.

As soon as it was demonstrated experimentally that simple, uncomplicated erysipelas is a disease attended by but little danger to life, the suggestion was near that, if the disease could be artificially produced in man by inoculation with pure cultures, the local and general conditions thus produced might prove useful in the cure or amelioration of some diseases not amenable to operative treatment and internal medication. Of 7 persons the subjects of incurable tumors, inoculated by Fehleisen with pure cultures, 6 developed typical erysipelas; in the seventh case the patient had passed through an attack of erysipelas only a few weeks previously, and was, in all probability, still protected against a new attack. This patient was inoculated a second time with a negative result. In other instances a second inoculation failed after a successful inoculation. The period of incubation was fixed at from fifteen to sixty-one hours. The microbe was found only in the lymphatic vessels and connective-tissue spaces, and when the culture was pure suppuration was never produced. Fehleisen has seen, by this treatment, a cancer of the breast become smaller, a lupus disappear almost completely, while a case of fibro-sarcoma and another of sarcoma were not materially affected by this method of treatment. Janicke and Neisser have recorded a death from erysipelas thus intentionally produced in a case of cancer of the breast beyond the reach of an operation. At the necropsy it was proved that the tumor had almost completely disappeared, and the microscopical examination of portions that had remained appeared to show that the tumor-cells had been destroyed through the direct action of the microbes. Biedert saw, in a child suffering from a sarcoma involving the posterior part of the cavity of the mouth and pharynx, the left half of the tongue, the naso-pharyngeal space, and the right orbit, the tumor disappear almost completely during an attack of erysipelas. Cases, on the other hand, have been reported in which, after an accidental or intentional attack of erysipelas, the tumor commenced to grow more rapidly. Neelsen reports a case of carcinoma of the breast, in which, after two severe attacks of erysipelas, the tumor not only commenced to grow faster, but at the same time the regional infection progressed also more rapidly.

Babtchinsky made the accidental discovery that the microbe of erysipelas is a direct antagonist to the virus of diphtheria. His son, while suffering from a most severe attack of diphtheria, was suddenly attacked by erysipelas. This complication, grave of itself, seemed to hasten the fatal termination of the case, and during the first few hours of the eruption the patient was much worse. But the next day the symptoms had much improved, and the patient made a rapid recovery. Following this indication Babtchinsky inoculated a second case of diphtheria with a culture of the microbe of erysipelas grown on agar-agar, and with an equally happy result. Since this time, of 14 cases of diphtheria treated with these inoculations, 12 resulted in recovery, and, as in the 2 cases resulting fatally the inoculation produced no effect, these negative results only tend to confirm the efficacy of the curative inoculations. It is remarkable that in all of the cases where erysipelas was produced artificially this disease pursued a mild course, and the patients recovered rapidly from both diseases.

Schwimmer gives an account of 11 cases of lupus, in all of which no improvement was observed after an intercurrent attack of erysipelas. In a case of keloid an attack of erysipelas was followed by marked improvement, and a lipoma underwent a similar favorable change from the same cause. Syphilitic lesions he saw temporarily benefited, while the erysipelas had no effect in permanently influencing the course of the disease.

Bruess gives an account of the effect of erysipelas on tumors in 22 patients. Among these 3 cases of sarcoma were permanently cured. Two cases of multiple keloid after burns were also cured. In 4 cases of lymphoma of the neck some of the glands became smaller and some disappeared. In 5 cases the erysipelas was artificially produced by inoculation with a pure culture. In 3 cases of carcinoma of the mamma 1 was not influenced by the disease, 1 became one-half smaller, and 1 was reduced to a small induration in the scar the size of a pea. A multiple fibro-sarcoma was greatly benefited, while an orbital sarcoma was not improved.

In view of the uncertainty of the result, and the not inconsiderable danger which attends the intentional form of erysipelas in patients debilitated by antecedent disease, it is safe to predict that no further inoculations will be made in man until, perhaps, future research will demonstrate a certain specific antagonistic action of the streptococcus of erysipelas against some other pathogenic microbes, the cause of grave diseases not amenable to successful treatment by less heroic measures.

MANNER OF INFECTION.

An intact skin or mucous membrane furnishes absolute protection against infection with the streptococcus of erysipelas. This microbe cannot reach the lymphatic vessels without an infection-atrium, which may be a small abrasion, a wound, blister, ulcer,—in fact, any breach of continuity in the skin or mucous membrane. Before antiseptic surgery was practiced, infection frequently occurred through accidental or intentional wounds. Antiseptic surgery has greatly diminished the frequency of traumatic erysipelas, but has not completely eradicated it, as an occasional case will occur in the hands of the most careful antiseptic surgeons. Even before the microbic cause of erysipelas was known, Trousseau, one of the closest of clinical observers, claimed that infection with the virus of erysipelas is only possible through some wound or abrasion of the skin; the latter may be so insignificant as to be unnoticeable and entirely overlooked by both patient and physician. Idiopathic or spontaneous erysipelas, so called, does not exist; every case of erysipelas is traumatic, in so far that by injury or disease the necessary infection-atrium must be created through which the streptococcus can reach the lymphatic vessels. In erysipelas without a tangible infection-atrium, infection occurs through a minute puncture or abrasion, which may, perhaps, never have attracted the patient's attention, and which has become invisible at the time the disease is first noticed. Infection, however, may also take place through a mucous membrane, through which the microbes enter the tissues in the same manner and under the same conditions as when infection takes place through the skin. One of the severest cases of erysipelas that ever came under my observation commenced in the pharynx, or tonsils, and, as the symptoms subsided here, a typical and severe facial erysipelas developed. As the patient was suffering at the same time from secondary syphilis, it is probable that the streptococcus of erysipelas entered the tissues through the secondary syphilitic lesions in the pharynx. In the tissues the streptococcus of erysipelas invades the lymphatic channels exclusively, and manifests here its specific pathogenic qualities.

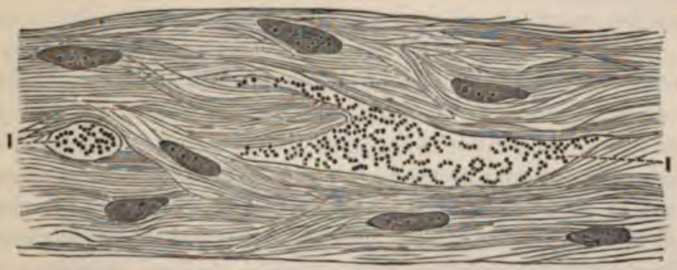

FIG. 88.—SECTION THROUGH SKIN NEAR THE MARGIN OF THE ERYSIPELATOUS ZONE. × 700. (*Koch.*)

1, 1, each a lymphatic vessel filled with streptococci in chains.

The erysipelatous inflammation is, in reality, a specific, progressive lymphangitis, the para-lymphatic tissues becoming affected by contiguity. Within the lymphatic channels the microbe multiplies, and diffusion of the infection takes place in the course of the lymphatic vessels, but does not always follow in the course of the lymph-stream. The lymphatic vessels are often found crowded with the microbe, which is destroyed in a short time, as with the subsidence of the inflammation the microbe disappears. According to Koch, and Fehleisen, the microbe is always found most numerous in the portion of the skin corresponding to the border of the inflamed area. At this point the lymphatics frequently appear completely blocked by dense colonies of this microbe, so that no lymph-corpuscles can be seen among them. As the inflammation extends to the surrounding connective tissue, some of the microbes leave the lymphatics and enter the connective-tissue spaces, where they come in contact with the inflammatory exudation. Within the lymphatic vessels the streptococci are found between the lymph and colorless blood-corpuscles; in the connective tissue they are found also within the protoplasm of leucocytes.

Metschnikoff maintains, in opposition to most of the modern authors, that the arrest of the extension of the erysipelatous inflammation is accomplished by phagocytosis. The accumulation of leucocytes in the inflamed tissues has, undoubtedly, a salutary effect in mechanically blocking the avenues through which infection takes place; but as most of the microbes are outside of, and not within, the leucocytes and lymph-corpuscles, it is difficult to conceive how limitation of the extension of the infection could be accomplished solely by phagocytosis. The microbes have a very short existence in the tissues; the inflammation which they initiate continues for some time after all microbes have disappeared. The ptomaines which microbes secrete produce protoplasmic alteration of the connective-tissue cells and the capillary blood-vessels, which prolong the inflammation beyond the period when the tissues are in a sterile condition. Others have claimed that self-limitation of erysipelas is due to destruction of the microbes by the high temperature which attends the disease. De Simone has recently shown that pure cultures of the streptococcus of erysipelas lose their power of reproduction if they are exposed for two days consecutively to a temperature of 39.5° to 41° C. Clinical experience, however, has demonstrated conclusively that erysipelas is not arrested in its course by a temperature of 40° C., or more. It appears that the streptococcus exhausts the soil of the nutrient material which it requires for its growth and reproduction in a short time. In the blood-vessels of the inflamed skin no streptococci can be found, but that they occasionally enter the blood-vessels is sufficiently evident from the occurrence of metastatic erysipelas, and the direct transmission of erysipelas from mother to fœtus by infection through the placental circulation. As the streptococcus of erysipelas produces its pathogenic effects in the lymphatic vessels, and diffuses itself through these channels in the tissues, it becomes obvious that in all cases infection takes place as soon as localization is effected in the superficial lymphatic structures, or in the spaces contributary to them, and in direct connection with an infection-atrium.

RELATION OF ERYSIPELAS TO PUERPERAL FEVER.

Obstetricians recognized the danger of exposing puerperal women to the infection which might emanate from erysipelatous patients long before the microbe of erysipelas was known. Since the discovery of the microbe by Fehleisen, this subject has attracted renewed attention, and positive knowledge has accumulated both from accurate clinical observation and from the fertile and more positive field of experimentation. Gusserow asserted, upon the basis of an extensive experience, that no direct etiological relations exist between the contagium of erysipelas and puerperal fever. He had under his care puerperal women suffering from erysipelas of the skin without any serious disturbances following in the genital tract. In 10 other cases, one of them occurring during an epidemic of puerperal fever, the erysipelas was observed as a complication of septic affections of the genital organs. Gusserow claims that in this case it cannot be claimed that erysipelas could have caused the puerperal affection, as the latter preceded the former. But another point could be raised, as it might be claimed that the septic processes should be made answerable for the occurrence of erysipelas. This author has studied this subject also by way of experiment. A pure culture of the streptococcus erysipelatosus, which had been tested and found reliable in producing erysipelas by the usual methods of inoculation, was injected into the peritoneal cavity of 2 rabbits; in 2 others it was applied to an open wound of the abdomen, and in the last 2 animals it was injected into the subserous connective tissue of the peritoneum. In all of these animals no effect was produced, and no pathological changes were detected at the point of injection when the animals were killed, some time after the inoculation. Gusserow looks upon the results of these experiments, if not as positive proof, nevertheless as strong evidence against the claim that erysipelas can cause puerperal sepsis. Winckel, an equally reliable and able observer, has come to entirely opposite conclusions. He cultivated from a parametritic abscess, which had developed after childbed, Fehleisen's streptococcus. Injections of this culture into rabbits produced typical erysipelas. The same author also observed erysipelas following in a puerperal woman suffering from suppurative perimetritis, pleuritis, and metro-lymphangitis. The patient died on the thirteenth day. The starting-point of the erysipelas could be traced to an ulcer of the vulva. Blood taken from the right side of the heart soon after death was inoculated upon a solid nutrient medium, and produced a culture of the streptococcus of erysipelas. The same culture was obtained by inoculations with fluids taken from the peritoneal and pleural cavities, the uterus, kidneys, and the liver. In 3 cases a culture thus obtained was injected into the peritoneal cavity of rabbits, and no peritonitis followed.

In 1 experiment the injection produced suppurative peritonitis. Guinea-pigs proved less susceptible to infection than rabbits. In white mice the inoculations were invariably productive of a fatal disease. From the results of these experiments the author claims that the virus of erysipelas is one of the most virulent puerperal poisons, and believes that they prove the casual relations of erysipelas to puerperal sepsis.

Doyen also found, both in mild and severe cases of puerperal fever, a streptococcus similar to the one described by Rosenbach and Fehleisen. He made some inoculations to determine the relationship between puerperal sepsis and erysipelas. The streptococcus found in the infected tissues of puerperal-fever patients caused erysipelas, and the streptococcus found in erysipelas developed puerperal fever. From his own observations and experiments the author arrived at the conclusion that the microbe of puerperal sepsis is the same as that of erysipelas. From a clinical and bacteriological stand-point it is evident that puerperal sepsis from infection with the streptococcus of erysipelas can only occur when the streptococcus is brought in contact with an absorbing surface in the genital tract; but when this takes place, and the microbes reach the enlarged lymphatic vessels of the puerperal uterus, the most violent and fatal form of puerperal sepsis is almost certain to follow.

RELATION OF ERYSIPELAS TO PHLEGMONOUS INFLAMMATION AND SUPPURATION.

Some difference of opinion still exists, among bacteriologists, with regard to the question whether the streptococcus of erysipelas possesses pyogenic properties. The majority of those who have studied this subject experimentally do not consider the streptococcus of erysipelas as a pus-microbe, and assert that when suppuration takes place in erysipelas it is the result of a secondary infection with pus-microbes, and, on this account, look upon phlegmonous inflammation as a complication, and not as a condition belonging to the erysipelatous process. Hajeck made careful investigations to show that the streptococcus of erysipelas is neither in form nor culture materially different from the streptococcus pyogenes, but he showed, also, that in 51 cutaneous or subcutaneous inoculations with a pure culture of the streptococcus of erysipelas in rabbits the result was always a superficial migrating dermatitis which resembled to perfection erysipelas in man, while similar injections with the streptococcus of pus produced a more intense and deeply-seated inflammation, which in almost every instance terminated in suppuration. The difference in the action of the two microbes on the tissues plainly demonstrated their non-identity. Microscopical examination of the inflamed tissue showed a still more important difference as far as the localization and local diffusion of the microbes were concerned. The microbe of erysipelas was always found with the products of inflammation *within the lymphatic vessels*, and only exceptionally in the connective-tissue spaces, which anatomically are only a part of the lymphatic system. The pus streptococcus penetrates the tissues more deeply; it is not only found in the lymphatic vessels and connective-tissue spaces, *but it migrates beyond the lymphatic channels and infects different kinds of tissue, thus giving rise to a more deeply-seated and more intense inflammation.* The streptococcus of erysipelas is found only exceptionally in the immediate vicinity of blood-vessels; *while the microbe of pus can always be seen arranged in radiate lines around vessels entering the adventitia, the muscular coat, and often even in the lumen of the vessel.* In man the same histological differences can be seen in the tissues the seat of erysipelatous and phlegmonous inflammation as in the artificial conditions in animals subjected to experiment, and the same pathological differences are also constantly found. The author asserts that Fehleisen was in error when he claimed that the formation of abscesses occurred independently of the erysipelatous infection. He affirms that in rabbits inoculated with the virus of erysipelas after the acute inflammation has subsided circumscribed small nodules which remain may suppurate, but suppuration never becomes diffuse, while after injection with cultures of the streptococcus pyogenes the inflammation assumes a phlegmonous type and the suppuration is always more diffuse. Hajeck maintains that under certain circumstances a circumscribed superficial suppuration can also take place in erysipelatous inflammation in man. When suppuration in a joint takes place, however, it is not caused by the erysipelatous infection, but is due to the presence of pus-microbes. Eiselsberg, Bonone, Bordini, Passet, and Simone are of the opinion that the streptococcus of erysipelas and the streptococcus of suppuration do not differ in their pathogenic effects.

Smirnoff found in 1 case of erysipelas the specific microbe in the metacarpo-phalangeal joint of the left hand, which was the seat of the disease. In the case of a man who had died of erysipelas, enormous colonies of the streptococcus were found in the right shoulder and knee joints. The synovial fluid injected into rabbits occasioned *erysipelas migrans.*

Rheiner found Fehleisen's streptococcus in all cases of traumatic erysipelas which he examined, but was unable to find it in 2 cases of gangrenous erysipelas following typhus. In these cases he found bacilli which he believed were identical with Klebs-Eberth's bacillus of typhus.

Kahlden, after a careful study of the recent literature on erysipelas, and the difference in opinion on the pathogenic properties of the streptococcus erysipelatosus, remarks that the subtility in the differences between the morphology and the cultures of the microbe of erysipelas and the streptococcus of suppuration is undoubtedly the reason why no uniformity of opinion exists in regard to their specific pathogenic effects, especially as to the possibility of Fehleisen's streptococcus producing suppuration. To this I might add that not every superficial diffuse inflammation of the skin is erysipelas, and not every abscess occurring during, or soon after, an attack of erysipelas should be considered as a product of the erysipelatous infection. The surgeon will do well to adhere to the teachings of Fehleisen, who is positive in his assertion that *the streptococcus of erysipelas never produces suppuration*, until more convincing proof shall have been furnished of the pathogenic identity of the streptococcus of erysipelas and the streptococcus of suppuration.

SYMPTOMS AND DIAGNOSIS.

Erysipelas, like most of the acute infectious diseases, has no well-marked premonitory stage, the attack being sudden and followed by all the symptoms which usher in an acute febrile affection. The period of incubation in man has been fixed at from fifteen to sixty-one hours by the inoculations which have been made to produce the disease artificially for therapeutic purposes. Inoculations prove successful if the skin is punctured with a needle the point of which had been dipped into a pure culture of the streptococcus. Such punctures have no visible lesion after a few hours,—a fact which readily explains the disappearance of a visible infection-atrium at the time the disease appears, in cases of erysipelas developing without a demonstrable breach of continuity in the skin.

In the adult the disease commences, almost without exception, with a chill which sometimes amounts to a severe rigor. Nausea and vomiting are often present during the first few hours. The chill is followed by a rise in the temperature, which in a few hours increases to 104° F. or more. The fever assumes a continuous type, and in uncomplicated cases the difference between the morning and evening temperature is slight. Headache, thirst, and complete loss of appetite are constant and prominent symptoms. The pulse is at first full and bounding and seldom exceeds 100 beats per minute. In severe cases delirium is present almost from the beginning, and continues until the fever subsides. Almost simultaneously with the appearance of the general symptoms, the skin in the immediate vicinity of the infection-atrium shows evidences of the existence of a superficial inflammation. The patient complains of a sense of tightness in the part, which is accompanied by a burning and itching sensation.

In traumatic erysipelas the wound presents no changes in its appearance; if suppuration is present the purulent discharge becomes somewhat diminished in quantity and the pus is rendered more serous. The skin around the seat of infection is firmer to the touch, and if the erysipelas has started from a wound infection has occurred from a certain portion of the wound, while the remainder shows no evidences which point to erysipelatous inflammation. The skin which is involved by the erysipelatous inflammation presents, almost from the beginning, a characteristic rose or crimson color. With the appearance of the typical discoloration the inflammatory exudation has reached its height. The color disappears under pressure, but upon the removal of the pressure no depression is left, showing that little or no œdema is present. The induration of the skin is most marked at the border of the erysipelatous zone, and disappears with the absorption of the inflammatory product and the return of the natural color of the skin. The margin of the zone is abrupt and distinct on the side of the healthy skin. The border of the erysipelatous zone is not straight, but irregular, and often *fan-like projections can be felt which project into the healthy skin, and, when present, they are characteristic, almost pathognomonic, of this form of dermatitis.* The degree of swelling varies according to the intensity of the infection and the anatomical structure of the part involved.

If the infection is intense and parts are implicated which are abundantly supplied with loose connective tissue, the swelling is greater than in cases where the infection is mild or the skin is stretched over firm, resisting parts. In facial erysipelas, for instance, the swelling is much greater around the orbits than in the scalp, because in the former locality the loose, cellular, connective tissue underneath the skin becomes swollen and œdematous from the escape into it of the inflammatory transudation.

The specific inflammation, starting from the point of infection, spreads continuously and uninterruptedly along the course of the superficial lymphatics, but is not limited to the direction of the lymph-current. The intra-lymphatic diffusion of the streptococcus is not a passive, but an active, process. As this microbe is non-motile, its transportation in a direction opposite to the lymph-stream can only occur by its reproduction. *The lymph-current in most, if not all, of the inflamed lymphatic vessels is temporarily arrested by the blocking of the interior of the lymphatic vessels with colonies of the streptococcus and the accumulation of lymph-corpuscles; consequently the colonies become fixed points from which new tissues are infected by their increase in size in all directions, owing to rapid reproduction of the microbe.* The fever continues until the infection comes to a stand-still. The intensity of the subjective symptoms does not always correspond with the temperature, as patients may feel quite well when the temperature registers 104° to 105° F., while others show evidences of serious disturbance with a much lower temperature. Small vesicles and large bullæ usually result from confluence of a number of vesicles. The contents of these blisters are first serous, but suppuration may follow later from the entrance of pus-microbes. Bullæ with hæmorrhagic contents denote a grave attack.

The duration of erysipelas is extremely variable. Genuine erysipelas may run a typical course and terminate in recovery in two days, or the disease may extend over a period of two weeks or more. The extent of surface successively invaded determines its duration. If it start from a wound of the hand it may extend along the forearm and arm to the shoulder, from here along the back to one or both of the lower extremities, and before such a large territory of skin has passed through all the stages of the disease more than four weeks may elapse. As soon as the disease ceases to migrate the general symptoms subside, and within a few days the skin returns to its normal condition, and the patient recovers his usual health in a remarkably short time,—a fact which tends to prove that erysipelas, in its uncomplicated form, does not impair the function of any of the internal organs to any considerable extent. Exfoliation of the skin is a usual occurrence. In the differential diagnosis we have to consider lymphangitis, erythema, phlegmonous inflammation, and thrombo-phlebitis. In lymphangitis from other causes than the streptococcus of erysipelas the inflammation follows larger lymphatic channels, which appear as red lines, and seldom, if ever, is the skin proper inoculated in the inflammatory process, while erysipelas is a combination of lymphangitis with dermatitis. Erythema appears as circumscribed points of inflammation in the skin with healthy tissue between, while, on the other hand, erysipelas shows no such interruptions, the inflammation being a continuous, uninterrupted process followed by speedy repair. Phlegmonous inflammation is accompanied by inflammation of the skin, which, in its external appearances, closely resembles erysipelas; but the differential diagnosis rests on the location of the primary inflammation, which is always the superficial lymphatics of the skin in erysipelas, and the subcutaneous tissue in phlegmonous inflammation. In phlegmonous inflammation the deep-seated inflammatory exudation is the primary pathological condition, and the lymphangitis follows as a secondary result, while in erysipelas the primary specific lymphangitis and dermatitis are primary conditions, and if the subcutaneous tissue become involved later on it must be regarded as a complication, and not as an integral part of the disease. Patients suffering from erysipelas complain of a smarting, burning, or itching sensation in the affected skin; phlegmonous inflammation is attended by severe pain, which is of a throbbing character. Thrombo-phlebitis, starting from a chronic ulcer of the leg, has often been mistaken for erysipelas, not only by laymen, but also by physicians. Thrombo-phlebitis is often attended by inflammation of the tissues around the inflamed vein and of the superimposed skin, but the inflammation follows in the course of the vein, and not in the course of lymphatics; at the same time the vein can be felt as a solid, tender cord.

CLINICAL FORMS OF ERYSIPELAS.

The clinical forms of erysipelas are identical in so far that they are all caused by the same microbe, and that the disease primarily consists of a specific lymphangitis and dermatitis; but they vary greatly, according to the location and structure of the part affected, the intensity of the infection, and the existence of complications.

Erysipelas Erythematosum.—This is the mildest form of erysipelas. It is described as erythematic because the affected skin shows but little swelling, and the affection appears more as an efflorescence than an inflammation. No bullæ form, and only slight exfoliation takes place during convalescence.

Erysipelas Bullosum.—In this form the inflammation of the skin is more intense and the swelling more marked, in consequence of which blisters or bullæ form underneath the cuticle. The pathological condition resembles a burn in the second degree. Removal of the cuticle leaves the papillary layer of the skin exposed. The bullæ often become the seat of secondary infection with pus-microbes, which transform the serous contents into pus. From such superficial foci of suppurative inflammation may develop what has been termed—

Phlegmonous Inflammation.—As we are not in possession of conclusive proof that the streptococcus of erysipelas possesses pyogenic properties, we can only explain the occurrence of phlegmonous inflammation of the tissues underneath the skin affected by erysipelatous inflammation by taking it for granted that the deep-seated phlegmonous inflammation is caused not only by the streptococcus of erysipelas, but by the accidental entrance into the tissues of microbes of suppuration. As soon as secondary infection with pus-microbes takes place the clinical picture of erysipelas is overshadowed or obscured by the suppurative inflammation. The typical general and local symptoms which characterize the erysipelatous inflammation give way to symptoms which indicate the existence of a diffuse suppurative inflammation. The temperature shows greater remissions, and the pulse becomes more rapid and feeble. The tongue is often red and dry, while all of the remaining symptoms point to intoxication from absorption of ptomaines produced in the tissues by the pus-microbes. The swelling of the part affected is no longer limited to exudation into the substance of the skin, but affects mainly the deep-seated tissues.

We have reason to believe that in most, if not in all, cases of phlegmonous erysipelas the secondary infection with pus-microbes takes place from a superficial suppurating focus as from a suppurating bulla, and that the microbes from here invade the subcutaneous connective tissue. The phlegmonous inflammation spreads with great rapidity, so that in a few days the skin of an entire extremity may become undermined with pus, the patient, in the meantime, having complained but little of pain. Such an extremity on palpation imparts the sensation of a partially filled diffuse abscess-cavity. The external appearances furnish, often, no reliable indications of the extent of the deep-seated destruction. If incisions are made at this time a large quantity of pus escapes, mixed with shreds of necrosed connective tissue, and examination reveals extensive destruction of the subcutaneous connective tissue and intermuscular septa. Phlegmonous inflammation, as a rule, does not attack tissues the seat of an erysipelatous inflammation, but the tissues weakened by this disease and infected with pus-microbes. A sudden increase in the temperature of patients suffering from erysipelas is often the first symptom which commences this complication, and such an occurrence should admonish the attendant to detect it early in order to subject it to timely and efficient treatment.

Erysipelas Gangrænosum.—This is an exceedingly grave form of erysipelas. Most of the authors are of the opinion that if the streptococcus of erysipelas multiplies with sufficient rapidity, in the interior of the lymphatic vessels and the connective-tissue spaces, so as to completely block these channels by its growth, a sufficient amount of ptomaines is produced to cause necrosis of the tissues, and under such circumstances the erysipelatous inflammation terminates in gangrene of the skin. This gangrene may take in circumscribed multiple patches, so that after separation and elimination of the dead tissue the skin presents a cribriform appearance, or it may involve a large district of the skin, and then give rise to extensive loss of this structure in case the patient survives the disease. As the gangrene often commences in the portion of skin covered by bullæ, it still remains an open question whether it results from the action of the streptococcus of erysipelas, or whether it is the result of a secondary infection with pus-microbes. Isolated patches of gangrene of the skin are met with in many cases that terminate in recovery, but extensive gangrene of the skin is always a serious complication, as it may result in death from septicæmia, or, if life is not destroyed, it at least greatly protracts the recovery, and often calls for a tedious treatment to restore the lost tissue by skin-grafting.

Erysipelas Metastaticum.—By metastatic erysipelas is meant the occurrence of an erysipelatous inflammation in an organ or a part where the process developed separately from the primary field of infection. If, for instance, erysipelas should appear in an extremity opposite to the one primarily affected, without extension of the disease across the skin of the trunk, it would furnish a good example of what is meant by metastatic erysipelas. Again, if during an attack of erysipelas of one of the extremities the patient should be attacked with symptoms of meningitis, and at the necropsy the streptococcus of erysipelas could be demonstrated in the inflamed envelopes of the brain, this would furnish another illustration of metastatic erysipelas. Two possibilities present themselves in explaining the occurrence of metastatic erysipelas. In the first place, colonies of the streptococcus in an active condition might reach a part distant from the erysipelatous inflammation with the lymph-current, and, meeting with favorable conditions, might establish an additional focus of erysipelatous inflammation, which, of course, would have to be necessarily in a part between the primary field of infection and the termination of the lymphatic vessels leading from the infected district. If no such connection can be established, then the metastatic process results from the entrance of streptococci in an active condition into the circulation and their localization in distant parts or organs by mural implantation upon the wall of capillary vessels prepared for their localization and reproduction. In most instances metastatic erysipelas is of such an embolic origin.

Erysipelas Migrans.—Migration of the inflammatory process is one of the characteristic clinical features of erysipelas. In ordinary cases migration is limited to the anatomical region affected. In cases of facial erysipelas the disease seldom spreads beyond the scalp, and in erysipelas of the extremities the disease usually subsides after it has extended over an extremity. Migrating erysipelas is that form of the disease where the erysipelatous inflammation extends from place to place, and from limb to limb. I have seen this form most frequently in infants, starting from the umbilicus or the external genital organs. I have seen it start from these points, ascend in an upward direction along the anterior aspect of the body, and, after reaching both shoulders, spread to the upper extremities, later to descend down the back, and finally terminate in the toes after traveling nearly over the whole surface of the body. Erysipelas of the extremities or trunk never extends to the face or scalp, while, in exceptional cases, erysipelas of the face assumes the migrating form. Migrating erysipelas is usually attended by only moderate swelling and slight constitutional disturbances. One peculiarity of this form of erysipelas is that the same regions may become involved a second time.

Erysipelas Facialis.—This is the so-called spontaneous or idiopathic form of erysipelas, as in most cases even close inspection does not reveal the existence of an infection-atrium. The disease usually commences in one of the alæ, or at the root of the nose,—localities where minute skin lesions are frequently produced, and localities which more than any other part of the face are exposed to infection by contact As far as its extension is concerned, facial erysipelas pursues the most typical course. The inflammation spreads toward the cheek and orbit on the side first affected, and then creeps across the bridge of the nose to the opposite side, to follow a similar course here. About the second or third day it reaches the forehead, and from here and the outer margins of the orbits it invades the scalp, to terminate usually about the end of a week at the nape of the neck. The chin and anterior aspect of the neck never become affected in facial erysipelas. Facial erysipelas is attended by considerable swelling, the eyes being often completely closed by the œdematous lids. Bullæ form frequently about the centre of the cheeks and the forehead. One of the dangers of facial erysipelas consists in the direct extension of the erysipelatous inflammation from the skin along the blood-vessels to the meninges of the brain. The meningitis under these circumstances is not a metastatic process, but the result of a direct extension of the inflammation from the skin to the meninges, along structures which connect them through the intervening skull. Patients who have suffered from facial erysipelas are not protected against subsequent attacks; in fact, experience has shown that they are more prone to infection in the future than persons who have never suffered from this disease. If the bullæ suppurate, there is always danger arising from suppurative thrombo-phlebitis, suppurative lepto-meningitis, and suppurative encephalitis,—fatal complications plainly attributable to secondary infection with pus-microbes.

Traumatic Erysipelas.—We have seen that, in the strict sense of the word, all cases of erysipelas are traumatic in their origin, in so far that infection never takes place through an intact skin or mucous membrane; consequently the disease never occurs without an infection-atrium, which may be a wound or a lesion of the surface through which the streptococcus gains entrance into the lymphatic channels. The expression "traumatic erysipelas" is still retained for the purpose of designating erysipelas as one of the numerous forms of wound complications. If a recent wound is infected with the microbe of erysipelas the disease develops within fifteen to sixty-one hours after the accident or operation.

The disease may occur in consequence of later infection at any time before cicatrization is completed, as granulations furnish no absolute protection against infection. I have seen the disease originate more frequently in granulating than in recent wounds,—a strong argument in support of the advice that *full antiseptic precautions should not be relinquished until the healing process is completed, if the patient is to be protected against an attack of erysipelas.* Another important fact should always be remembered: that *small wounds are more frequently attacked by erysipelas than large wounds, because the latter receive more careful attention, and are, as a rule, subjected to more rigid antiseptic treatment.*

PROGNOSIS.

Simple uncomplicated erysipelas is not a fatal disease unless it attacks infants or persons debilitated by age or antecedent diseases. Death is caused more frequently by complications. The most common fatal complications are suppurative inflammation at the seat of erysipelatous inflammation, or metastatic suppuration in distant parts or organs, resulting from secondary inflammation with pus-microbes, or, finally, extension of the erysipelatous inflammation to important organs, as the brain or its envelopes, in cases of facial erysipelas, or the occurrence of metastatic erysipelas in vital organs from embolic processes. The prognosis is, therefore, based largely upon the absence or presence of complications, which must be carefully sought for in all cases where general or local symptoms point to their existence. The temperature, pulse, and condition of nervous and digestive organs furnish important and valuable prognostic indications.

TREATMENT.

The number of specifics which at different times have been recommended in the local and general treatment of erysipelas must throw doubt upon the efficacy of any local applications or internal remedies in arresting the further progress of erysipelas. At the same time it must not be forgotten that uncomplicated erysipelas is a disease which tends to spontaneous recovery, and seldom proves fatal, even if it is allowed to pursue its own course, unaided by any local application or internal medication. The erysipelatous inflammation is of short duration, and passes through its different stages uninfluenced by local or general treatment. Since its microbic origin has been suspected different methods of treatment have been recommended to arrest the further progress of the disease by destroying or rendering inert the primary cause. Hueter aimed at the destruction of the specific microbe by injecting at different points at the border of the erysipelatous zone 5 to 6 cubic centimetres of 3-per-cent. solution of carbolic acid. This method of treatment in the hands of others has been followed almost without exception by negative results. It is possible that subcutaneous injections of a 1-to-1000 solution of corrosive sublimate in non-toxic doses would yield better results. The continued application of cold, even of an ice-bag, has been found useless in arresting the disease. As it has been found that a temperature of over 40° C. continued for two days has at least an inhibitory effect on the growth of the streptococcus of erysipelas in artificial nutrient media, it would appear rational to resort to hot antiseptic compresses in the local treatment of erysipelas. If the area involved is limited, a compress, saturated with a weak hot solution of corrosive sublimate, would answer a most admirable purpose. If a large surface is affected some of the weaker germicidal solutions could be used in the same manner. Moisture and heat relieve also the burning, smarting sensation more promptly and efficiently than the different filthy oils and salves which have been employed. Application of tincture of iodine, muriated tincture of iron, and solutions of nitrate of silver are worse than useless, because they destroy the skin, which should be carefully preserved in order to protect the patient against secondary infection with pus-microbes.

Recently Kraske recommended multiple minute incisions or, rather, scarifications in the skin, at the peripheral zone of the erysipelatous inflammation, for the purpose of preventing further extension of the disease. If the skin is first rendered aseptic, and subsequent secondary infection is guarded against by the application of a reliable antiseptic, this treatment may prove valuable in modifying the progress of the disease. After scarification a hot, moist, sublimated compress should be applied, to be immediately replaced by another when removed. The external use of ichthyol, so highly recommended by Nussbaum, has proved useless in my hands, both in relieving suffering and in preventing the extension of the disease.

Wölfler has recently called attention to the value of the mechanical treatment of erysipelas. He has published 18 additional cases of erysipelas treated by pressure of strongly adhesive plasters. After the plaster is applied the disease extends into the compressed parts of the skin, which swell considerably and remain swollen for several days, and then both the swelling and the fever diminish. He recommends that by way of precaution a second line should be commenced several centimetres distant from the first. The part must be carefully inspected once or twice daily in order to detect any loosening of the plaster. Occasionally the erysipelatous inflammation extends in diminished intensity for a short distance beyond the first line of plaster, but this does not last long. This method of treatment is at least harmless, and if future experience should prove, as it probably will, that it will not succeed in arresting the local extension of the disease, it will at least provide an efficient protection for the inflamed skin.

Phlegmonous inflammation and metastatic suppuration should be prevented, as far as possible, by the employment of such measures as will guard against the formation of suppurating foci in the inflamed skin. Bullæ should be evacuated as soon as they form by puncturing with an aseptic needle, carefully preserving the cuticle as a protection against the entrance of pyogenic microbes. Infiltrated air should not reach the inflamed skin, and for this purpose it should be covered either with an antiseptic, moist compress, or a thick layer of antiseptic cotton. The skin is disinfected in advance of the extension of the disease, and is subsequently protected against additional infection by applying a hot, moist, antiseptic compress, or by covering it with antiseptic absorbent cotton. If suppuration take place in the interior of bullæ the cuticle should be removed, after which the surface is carefully disinfected by irrigation with a germicidal solution, followed by an application with a 10-per-cent. solution of chloride of zinc, and further infection prevented by an antiseptic dressing. If phlegmonous inflammation develop in spite of these prophylactic measures, early and free incisions are made, free drainage established, and a subsequent treatment followed out appropriate for phlegmonous inflammation not complicated by erysipelas. Gangrene of the skin is to be treated by applying a hot antiseptic compress until the dead tissue is eliminated, when the defect is replaced by skin-grafting. Internal medication has even been less satisfactory than the local measures in the treatment of erysipelas. During the febrile stage the administration of the tincture of ferric chloride and the mineral acids does more harm than good. If the temperature is high, a daily antipyretic dose of quinine is indicated, and exerts a favorable influence upon the local process and the general condition of the patient. If the patient is restless a full dose of Dover's powder should be given at bed-time. Symptoms of prostration are met early by the use of a substantial wine or some other alcoholic stimulant.

Symptoms of collapse are treated by administering internally 1½ grains of camphor every hour, or the same amount of the drug is dissolved in oil of sweet almonds and injected subcutaneously every half-hour or hour until symptoms of intoxication, delirium, and reduction of the pulse to 50 or 55 beats per minute are produced. The camphor treatment in grave cases of erysipelas was introduced by Pirogoff, and has yielded excellent results when the threatening symptoms point to an enfeebled heart.

ERYSIPELOID.

A new form of infective dermatitis, which in many respects resembles erysipelas, has been recently described by Rosenbach under the name of "erysipeloid." It attacks usually the fingers and exposed portion of the hand, and is most frequently met with in persons who handle game or dead animals, as cooks, butchers, fish-dealers, and tanners. The affection starts from some minute abrasion of the skin as a bluish-red infiltration, which slowly advances in an upward direction. The inflamed parts are the seat of a burning, smarting sensation. While the skin at the point of infection returns to its natural condition and color, the zone of infiltration becomes larger, as it continues to spread until the disease appears to exhaust itself in the course of from one to three weeks. The infectious material which produces this disease is contained in decomposing animal substances. Infection may take in any abraded part of the body which comes in contact with material containing the virus. The temperature remains normal, and the general health is not affected. The inflammation travels very slowly, so that if infection take place in the tip of a finger it reaches the metacarpo-phalangeal joint in about eight days, and during the second week it spreads over the back of the hand, from where an adjacent finger may become affected, the extension then taking a direction opposite to the lymph-current. Repeated experiments to obtain a pure culture of the microbe failed, until in November, 1886, the author succeeded in cultivating it upon gelatin from a case in which the disease could be traced to infection from old cheese.

The author injected a pure culture under the skin of his own arm at three different points. After forty-eight hours he experienced a smarting, burning sensation at the points of injection; at the same time a circumscribed redness appeared around each puncture, which soon became confluent. On the fifth day each puncture was surrounded by a zone of inflammation the size of a silver dollar, somewhat elevated above the niveau of the surrounding skin. While the centre of this red patch became pale, the zone of inflammation continued to enlarge. In the inflamed skin the capillary vessels could be seen dilated,—a condition of the circulation which imparted to the tissues an arterial hue with a slight tinge of brown, while inside of the zone the color was a livid brown. In the skin which had returned to its normal pale color slight suggillations appeared, as though some of the red blood-corpuscles in the tissues had been destroyed during the progress of the disease. The inflammation appeared to have completely subsided on the eighth day, when the smarting sensation returned, and a new zone appeared around the old one. On the tenth day the area measured in its transverse diameter 24 centimetres, and in the parallel direction of the arm 18 centimetres.

After this the affection disappeared permanently. During all this time the general health remained unimpaired, and the temperature varied from 36.8° to 37.2° C. A microscopical examination of the pure culture showed that it was composed of swarms and heaps of irregular, round, and elongated bodies somewhat larger in size than the staphylococcus. The author first believed that these bodies were cocci, but later he saw a net-work of intertwining threads, and decided that they were thread-forming microbes. In old cultures the threads were very abundant, and arranged in every possible way and direction. These threads appeared as though branches were given off, but on closer examination it could be seen that no organic connection existed between them. Terminal spores at the tips of the threads were numerous and could not be stained. Neither the microbes nor the threads manifested motile power in the culture, or when suspended in water; a gelatin culture became visible on the fourth day as a delicate cloud, which increased in size very slowly at a temperature of 20° C. The older cultures change into a brownish-gray color, and then resemble the culture of the bacillus of septicæmia in mice. In cultures 4 months old the growth was not entirely suspended. The author, as yet, has not given a name to this microbe, but believes, on botanical grounds, that it belongs to the "cladothrix" variety of micro-organisms. He wished to ascertain the action of this microbe on lupus, but in several cases in which it was tried the inoculations failed. Erysipeloid is a harmless form of infection, and subsides spontaneously in the course of two or three weeks. I have seen a number of cases in persons handling fish and game, where the affection started in one of the fingers, extended slowly as far as the dorsum of the hand, and then gradually invaded an adjacent finger and the back of the hand as far as the wrist. In the cases that have come under my observation the inflammation never extended beyond the wrist. The disease is self-limited, and its local extension is not arrested by any topical applications.

CHAPTER XV.

TETANUS.

THE wound-infective diseases in which the microbes or their ptomaines act upon the central nervous system are represented by tetanus and hydrophobia. The specific microbes which are the cause of these diseases produce no gross pathological changes in the brain or spinal cord, but the minute tissue changes cause a central irritation, which is manifested by spasm of certain definite muscular groups. Tetanus is an infective disease in which the specific microbic cause exerts its pathogenic action on the central nervous system, and which is clinically characterized by spasm and rigidity of definite muscular groups.

BACTERIOLOGICAL STUDIES.

The classification of tetanus with the infectious diseases is of recent date, but the infectious nature of the disease was well known and established before the discovery of the bacillus tetani. In 1859 Bétoli related the case of a bull that died of tetanus after castration. Several slaves ate some of the flesh of the dead animal, and of these 3 were (in a few days) seized with tetanus and 2 of them died. He adds, further, that in Brazil, where this occurred, the flesh of animals dead of tetanus is generally regarded as capable of transmitting the disease. In 1870 Auger reported a case in which a horse had spontaneous tetanus, after which 3 puppies which had been in the same stable were also affected. Larger, in 1853, saw a woman who had a fall while cleaning a farm-yard, causing a slight wound of the elbow. Four weeks later she was seized with tetanus, and on investigation it was found that a horse affected with that disease had been in a stable opening into the yard where she fell. He also mentions another circumstance which strongly points to the infectious nature of tetanus. In a small village, where tetanus was previously unknown, 5 cases appeared in eighteen months under quite different climatic conditions. Of these, 1 had been taken to a hospital, after which 2 others in the same ward became affected with the disease. In 1884 Carle and Rattone produced the disease artificially in animals by inoculations with pus from tetanic patients. Nearly at the same time the real microbic cause of tetanus was discovered by Nicolaïer and Rosenbach. Nicolaïer showed the exogenous origin of the disease by finding a bacillus in earth, which produced tetanus in animals when injected into the tissues. Rosenbach found the same bacillus in the pus of a patient suffering from traumatic tetanus. The identity of the bacillus of tetanus with Nicolaïer's bacillus of earth tetanus was demonstrated in Koch's laboratory, April 10, 1887.

Bacillus Tetani.—Rosenbach describes the bacillus as an anaërobic micro-organism which presents a bristly appearance, with a spore at one of its extremities which gives it the resemblance to a pin, or drum-stick.

According to Kitasato the bacilli produce spores in thirty hours in cultures kept at a temperature of the body. They possess great resistance to heat, as they have been found active after an exposure of one hour to 80° C. of moist heat, but they are destroyed by placing them in a sterilizer heated to 100° C. for five minutes. The bacillus has been found in different kinds of surface soil and in street-dust. In man it has been found in tetanic patients in the wound-secretions, in the nerves leading from the seat of infection, and in the spinal cord.

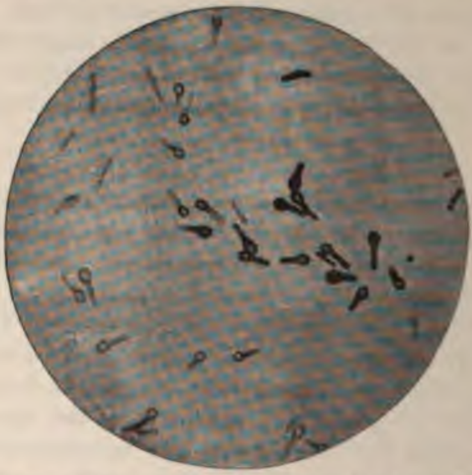

FIG. 89.—TETANUS BACILLI. SPORE-BEARING RODS FROM AN AGAR CULTURE. MOUNTED PREPARATIONS, STAINED WITH FUCHSIN. × 1000. (*Fränkel-Pfeiffer.*)

Cultivation.—Rosenbach found it impossible to obtain a pure culture; although he resorted to fractional cultivation, it was found that the last culture was still contaminated by one or more additional microbes. Fluegge claimed to have obtained a pure cultivation by heating for five minutes the mixed culture to 100° C., but after this procedure the bacillus was incapable of further propagation. After many trials it was found that sterilized solid blood-serum was the best soil for the propagation of the bacillus outside of the body. Both Nicolaïer and Rosenbach observed the anaërobic nature of the bacillus, as it was found impossible to obtain a culture by streak inoculations, or in any other manner by which oxygen could not be excluded. The culture appeared slowly, as a delicate, whitish-gray film, in the track of the stab inoculation, below the surface of the culture substance. By a long series of cultures, Rosenbach finally succeeded in eliminating all other microbes, with the exception of a bacillus of putrefaction. The growth of the bacillus takes place most readily at an equable temperature of 37° C. (98.6° F.), and becomes first visible about the third day in the depth of the culture media. Kitasato has finally succeeded in obtaining a pure culture of the bacillus of tetanus from pus taken from a patient suffering from this disease. As the bacillus will only grow where atmospheric air can be excluded, he exposed his cultures to hydrogen gas with complete exclusion of oxygen. Mixed cultures, which had been kept for several days in the incubator, were then exposed for half an hour to a temperature of 80° C. Further growth was then obtained upon plate cultures in closed glass vessels filled with hydrogen gas. By heating the mixed culture to 80° C. he destroyed all microbes with the exception of the bacillus of tetanus, which, later, was cultivated upon solid nutrient media in an atmosphere of hydrogen gas. At a temperature of 18° to 20° C., a visible culture appeared at the end of a week. If the temperature was increased to blood-heat the bacilli and spores developed more rapidly.

Inoculation Experiments.—Nicolaïer produced tetanus in rabbits and mice, experimentally, by inoculations with different kinds of surface soil. Out of 140 experiments, in 69 a disease was produced identical with tetanus in man. In the pus, at the point of inoculation, bacilli and micrococci were constantly found. Among the bacilli one form was constantly present; this bacillus resembled in appearance and culture the bacillus of septicæmia in mice, but was more slender. This bacillus was found in isolated places in the connective tissue, but could not be found in the muscles, nerves, and blood. Earth sterilized by exposing it to a high temperature for an hour proved harmless, showing conclusively that the contagium of tetanus had been destroyed. Inoculations with pus taken from tetanic animals were most successful. Inoculations with mixed cultures grown in solidified blood-serum yielded positive results.

Rosenbach made his experiments with mixed cultures grown from pus, taken from the line of demarcation of a case of frost gangrene, in a patient who had died of tetanus. The inoculations proved successful. Bonone reports the case of a man suffering from paraplegia, the result of disease of the spine in the dorsal region, complicated by an extensive sacral decubitus, the seat of phlegmonous inflammation, who was suddenly attacked by tetanus, which proved fatal in two days. One hour after death a small portion of the infiltrated tissue around the gangrenous part was removed, and after reducing it to a fine pulp by trituration he injected it under the skin of a rabbit. Twenty-two hours after inoculation the animal died with well-marked symptoms of tetanus. The products of inflammation from the point of injection thrown into the subcutaneous tissue of other animals produced the disease, while intravenous injections proved harmless. The gravity of symptoms following subcutaneous injections was commensurate with the quantity of fluid injected. Guinea-pigs proved less susceptible to infection than rabbits. In the pus taken from the dead tissue he found, besides the usual pus-microbes, a bacillus which resembled in every respect the one described by Nicolaïer and Rosenbach. Hochsinger made his observations on a case of tetanus which proved fatal on the fifth day. The day before the patient died blood was abstracted from a vein, under strict antiseptic precautions, for microscopical and bacteriological study. No micro-organisms could be found in it. With the greatest care sterilized, solid blood-serum was inoculated with the blood, by making, with the needle, both superficial streaks and deep punctures. The nutrient medium was kept at a temperature of 37° C. (98.6° F.). On the third day a white, cloudy streak marked the direction of the deep punctures, while the superficial plant remained sterile. On the third day a portion of the culture was removed and stained with aniline gentian, and the characteristic bacillus was found. A large rabbit was infected by injecting blood obtained from the patient during life. The blood was diluted with sterilized water, and a syringeful of this mixture was injected under the skin in the iliac region, and half of this quantity under the skin of the left thigh. The next day the animal was quite ill and unable to use the left hind-leg, which was dragged along in walking. At this time great nervous excitability was observed, the exaggerated reflex symptoms being especially well marked in the posterior extremities, which, on the slightest touch, were thrown into clonic spasm. On the following day the animal was found dead. A few hours before death well-marked symptoms of tetanus developed. Injections of blood from this animal produced no results in other rabbits, and culture experiments were equally fruitless. A syringeful of inspissated blood of the patient, kept for three weeks, thrown under the skin of a white mouse, was followed by a fatal attack of tetanus, while a second animal inoculated in a similar manner with one-half of this quantity remained perfectly well.

Fluegge had before observed that by injecting blood from animals rendered tetanic by inoculation it was necessary to use a large quantity in order to reproduce the disease in other animals, and even by doing so the result was not always satisfactory. It appears that the blood of tetanic patients possesses greater toxic properties than the blood of animals suffering from the same disease. Hochsinger also made inoculations with the mixed cultures. A syringeful of a liquid culture was injected into the subcutaneous tissue of a medium-sized rabbit. The next day the reflexes were increased, respiration more rapid, and the animal appeared otherwise quite sick. On the third day the posterior extremities were stiff, the animal dragging them in walking; reflex irritability enormously exaggerated. On the fifth day the animal died, with well-marked symptoms of tetanus. A number of similar successful experiments are reported by the same author. In rabbits, Fluegge estimated the stage of incubation at from three to five days, and the duration of of the disease, from the time the first symptoms were noticed to the fatal termination, from five to seven days.

Beumer gives an accurate and able description of his studies in 2 cases of tetanus. The first case occurred in a mechanic, who injured himself under the nail of the right middle finger with a splinter of wood. Eight days after the injury, the patient having had but slight pain in the finger, pains appeared in the neck and muscles of the back. The next morning spasms of the muscles of the chest, abdomen, and jaw developed. These attacks occurred at intervals of an hour and a half. Four days later the lower extremities were affected, also the upper, but in a less degree. An incision was made and the foreign body removed, which was followed by the escape of a drop of pus; death on the fourth day. The second case was a boy 6½ years old, who was brought into the clinic with well-marked symptoms of tetanus, and who lived only a few hours after his admission. The author obtained some of the dust and splinters of wood from the place where the mechanic had injured himself, and inserted small particles under the skin of mice and rabbits. In all experiments the animals were attacked with tetanus in from two to three days after inoculation, and during the third or fourth. The spasms were always noticed first in the muscles nearest the point of inoculation. A fragment of tissue from the sole of the foot was taken from the boy, and small particles of it inserted into the subcutaneous tissue of 6 mice. In all of these symptoms of tetanus appeared after two days, developing gradually into general convulsions and death.

The same results were obtained in mice and rabbits by inoculations of particles of dust taken from the spot where the boy sustained the injury. The same author also made numerous experiments with different kinds of earth. Of 10 experiments with soil taken from the ocean-beach, tetanus followed in only 2. On the other hand, of 10 inoculations with garden-earth and street-dust, all proved successful but 1.

Of the greatest scientific and practical interest are the observations made by Bonone, in reference to the causation of tetanus by infection with earth containing the bacillus discovered by Nicolaïer. He had an opportunity to observe a number of cases of tetanus after the earthquake at Bajardo. Of the 70 persons injured in the ruins of the church, 7 were attacked by tetanus. From bacteriological investigations in connection with these cases, he came to the same conclusions in regard to the cause of the disease as Nicolaïer, Rosenbach, Fluegge, and Beumer before him. Of special importance is the observation made by him, that the secretions from the wounds and the exudation from the part, the seat of tetanic convulsions, when dried and preserved between two sterilized watch-glasses, retained their virulent properties for at least four months. All animals inoculated with dust from the *débris* in the interior of the church were attacked with tetanus. Control experiments with dust from the ruins at Diano-Marina were always followed by negative results. Of the many persons injured during the same earthquake at this place, not one was attacked by tetanus.

Ohlmüller and Goldschmidt made a thorough bacteriological investigation of a case of tetanus following complicated fracture of the right thumb. The disease appeared the day following the injury, and proved fatal in seventeen hours. Soon after death inoculation experiments were made with blood taken from the heart and spleen, and pus from the seat of fracture. The cultures were grown in solid blood-serum kept at a temperature of 38° C., (100.7° F.). The tubes containing blood from the heart and spleen remained sterile, but the nutrient media infected with pus showed signs of growth. The bacilli which were detected resembled those of mouse-septicæmia, only somewhat larger in size. In addition to these microbes streptococci and a thick bacillus were found. Two mice were inoculated with this mixed culture. Twelve hours after infection tetanus developed, followed by death in seventeen hours. The spasms commenced in the tail, extended to the posterior extremities, and then gradually advanced in a forward direction. From these animals blood-serum was taken, with which other mice were infected. Again, tetanus was produced, and successful cultivations were made of 2 mice of equal size and age; 1, which received one portion of a culture, died of tetanus on the ninth day, while the other, which received a dose three times as large, died on the third day. Of 3 cases of tetanus which recently came under the observation of Lumniczer, he was able to demonstrate the microbic origin in 1. In this case the attack followed a gunshot injury. After the disease had developed fragments of hemp were removed from the canal made by the bullet, and in them the characteristic bacillus was found. Cultures were made to the tenth generation, and with them animals were inoculated, and tetanus was invariably produced. Pus taken from abscesses produced at the point of inoculation contained the bacillus, and inoculation experiments made with it yielded positive results. Cultures made from the blood or organs of the tetanic animals remained sterile. Inoculations with blood from these animals proved harmless.

Kitasato experimented with a pure culture of the bacillus of tetanus on mice, rats, guinea-pigs, and rabbits, and never failed in producing the disease, provided a sufficiently large dose of the culture was administered. In mice the disease appeared, without exception, twenty-four hours after the inoculation, and proved fatal in two to three days. The tetanic convulsions were first always local, appearing first in the muscles nearest the point of inoculation, and becoming gradually more diffuse. He was unable to find the bacillus at the seat of inoculation, the blood, or in any of the internal organs. He is of the opinion that if tetanus is produced by inoculation with a pure culture the bacilli do not remain in the body for any length of time, but are rapidly eliminated. The experiments and clinical observations which have just been quoted furnish conclusive proof that tetanus is a microbic disease, and that the bacillus of tetanus discovered by Nicolaïer and Rosenbach is its essential cause. Whether cultivations from chronic cases of tetanus can produce an acute and rapidly-fatal attack in animals remains to be determined. In this direction I have recently made an observation which, if not convincing, is at least very suggestive. A boy 15 years of age, previously in good health, was attacked with acute osteomyelitis in the lower extremity of the femur. The surgeon in attendance trephined the bone just above the external condyle during the first few days, and before an abscess had formed in the soft parts. A few days after the operation trismus set in, followed by typical chronic tetanus. Six weeks later the patient entered the Milwaukee Hospital, and was placed under my charge. At this time the patient had become emaciated to a skeleton.

Trismus and opisthotonus were well marked, and the lower extremities were rigid and fixed in the extended position. The slightest touch, or a draught of air in the room, would bring on intense convulsive attacks for several minutes, attended by excruciating pain. Profuse fetid discharge at the site of operation; pulse, 140; temperature, from 99° to 101° F. (37.3° to 38.8° C.). Believing that the primary infection had taken place through the operation wound, and that the osteomyelitic products served the purpose of a nutrient medium for the bacillus tetani, I determined to operate in spite of the grave symptoms. As the spinal cord at this stage of the disease was necessarily the seat of the intense congestion, I resorted to chloroform as an anæsthetic in preference to ether. The usual operation for necrosis of the lower end of the femur was made, and a large triangular sequestrum removed from the lower and posterior aspect of the bone. The involucrum was defective, and its inner surface was found lined with a thick layer of flabby granulations. Gelatin tubes were inoculated with blood, pus, and granulation tissue. The tube inoculated with blood remained sterile, while the two remaining tubes showed a copious growth of staphylococcus pyogenes albus, which rapidly liquefied the gelatin. A portion of the granulation tissue was disinfected with a weak solution of carbolic acid, dried between layers of antiseptic gauze, and inserted under the skin of a full-grown, large rabbit. No suppuration followed, and the animal remained perfectly well for six weeks, when both posterior extremities became rigid and could not be used in walking. The next day tetanic convulsions affecting the muscles of the back and all the limbs appeared, and on the fourth day death supervened.

The interesting features in this case are that the patient recovered from the tetanus after a long illness, extending over three months; that marked improvement followed the operation, which had for its object thorough disinfection of the infection-atrium; and that the inoculation with granulation tissue in the rabbit was followed by an acute attack of tetanus after an incubation stage extending over six weeks. In the experiments related above the animals were inoculated with cultures, earth, other infected foreign substances, fragments of diseased tissue, or with wound-secretions from tetanic patients; the stage of incubation rarely extended over two or three days, and often the spasms appeared in eighteen to twenty-four hours, and the disease produced death in from two hours to three days.

The same question has been raised in connection with the pathogenic action of the bacillus of tetanus as with pus-microbes: Is the disease of which it is the specific cause due to the presence of the microbe, or the ptomaines which it elaborates in the tissues?

Ptomaines of the Bacillus Tetani.—Brieger, by his indefatigable labors, has demonstrated beyond all doubt that the ptomaines of the bacillus of tetanus cause tetanic convulsions. Strychnia in toxic doses produces a condition which, so far as the muscular spasms are concerned, closely resembles tetanus. If this and other drugs belonging to the same group can act upon the spinal cord in such a manner as to cause spasms and muscular rigidity, we should, *à priori*, expect that if the microbe of tetanus produce ptomaines in the tissues these might produce the same effect on the cord, and that the symptoms are produced by them and not by the direct action of the microbe. Nearly all authorities are agreed that the bacilli present in the blood of tetanic patients are few, and in animals in which the disease was produced artificially the blood was often found sterile. More microbes have been found at the seat of primary infection, and in the tissues between it and the spinal cord, than in the blood itself,—another proof that the direct cause of the disease is the product of the microbes, and not the microbes themselves. Brieger has succeeded in isolating four toxic substances from mixed cultures of the tetanus bacillus in sterilized emulsion of meat. The first, *tetanin*, in doses of a few milligrammes, administered subcutaneously in mice, produced the characteristic symptoms of tetanus. The second, *tetanotoxin*, causes, first, tremors; later, paralysis and convulsions. The third, *muriate of toxin*, has not been designated by a special name; it produces also well-marked symptoms of tetanus, but, besides, excites the salivary and lachrymal glands to increased functional activity. The last, *spasmotoxin*, produces severe clonic and tonic spasms, which prostrate the animal at once. Besides meat-emulsion, the contused brain-substance from horses and cattle was used; also cows' milk mixed with carbonate of lime. It seems that the culture substance determined, to a certain extent, the kind of toxin which was produced; thus, in cultures grown in brain-substance, besides the tetanin, tetanotoxin was found in greatest abundance; old cultures, in which the tetanus bacilli were dead, produced none of these toxic substances.

The same author has very recently been successful in isolating tetanin from the amputated arm of a patient the subject of tetanus. The disease had developed a few days after a severe crushing injury of the hand and forearm. The first symptoms manifested themselves in the morning, and at 12 o'clock (noon) the operation was performed; at 5 o'clock on the same day the patient expired suddenly during one of the tetanic convulsions. The bacilli of tetanus were found in the serum taken from the œdematous portion of the forearm, in connection with other bacilli of different length,—staphylococci and streptococci. Serum containing these microbes injected under the skin of mice, guinea-pigs, and rabbits invariably produced tetanus. On the other hand, a dog treated in the same manner, as well as after injections of tetanin, remained well. A horse inoculated with a culture of bacilli in meat-emulsion showed no symptoms of tetanus, but an abscess formed at the point of inoculation. The infiltrated tissues of the amputated arm planted on sterilized meat-emulsion, solid blood-serum, and emulsion made of the flesh of fish, yielded, besides ammonia, only tetanin; no trace of tetanotoxin, spasmotoxin, nor the unnamed toxin which could be obtained from Rosenbach's bacillus. A moderate dose of tetanin injected into the subcutaneous tissue of a horse produced muscular contractions which lasted for a considerable length of time, but the characteristic symptoms of tetanus, as witnessed in horses suffering from tetanus, did not appear.

ETIOLOGY.

The clinical and experimental researches just quoted demonstrate that the bacillus tetani is found in the wound-secretions, the tissues, and, in some instances, in the blood of tetanic patients, and that tetanus in animals can be produced artificially by injections of wound-secretions of tetanic patients, or by using mixed or pure cultures,—facts which have firmly established the microbic nature of the disease. The essential cause of tetanus is the bacillus first discovered by Nicolaier in earth, and by Rosenbach in the wound-secretion of a tetanic patient.

Period of Incubation.—The period of incubation, both in man and animals, appears to be extremely variable, in some instances lasting only twenty-four hours, while in others weeks may elapse between the time of infection and the first manifestations of the disease. This may depend on one of three things: 1. The number of bacilli introduced may be so small that a much longer time is necessary before active symptoms are produced than if a larger quantity had been introduced, as Watson-Cheyne has shown that in animals the injection of a limited number of the bacilli of tetanus produced no symptoms. 2. The location of the infection-atrium and anatomical characteristics of the tissues surrounding it may influence the time which is necessary to develop the disease. 3. Brieger's investigations have shown that tetanic convulsions in animals are produced by injections of tetanin,—one of the toxic ptomaines derived from cultures of the bacillus of tetanus; and it is more than probable that the active symptoms of tetanus in man are due not to the presence in the tissues of the bacillus, but to the toxic action of the ptomaines on the spinal cord; so that the duration of the period of incubation is further modified by the capacity of the infected tissues to yield the different ptomaines. The degree of virulence of the bacillus of tetanus must certainly play an important part, not only in determining the duration of the incubation stage, but also the gravity of the disease.

Specific Microbic Cause.—There can be no doubt that both the acute and chronic forms of tetanus are caused by the same microbe, and that the clinical difference depends upon the degree of virulence of the primary cause, on the one hand, and the degree of susceptibility of the individuals to tetanic infection, on the other.

In reference to the susceptibility to infection with the bacillus of tetanus, it has been shown by reliable statistics that the colored races, under the same conditions, are attacked more frequently by tetanus than the Caucasians. Inoculation experiments have shown that the greatest difference exists among different kinds of animals in this respect, and there is no reason why the same difference of susceptibility to this disease should not exist in the human species. As the natural habitat of the bacillus of tetanus is the soil, we can readily understand that the disease should occur more frequently in some localities than in others, and why it is more prevalent in southern than northern climates. The excretions and cadavers of tetanic animals may infect the soil, where, under favorable conditions, the bacillus may multiply, and in this manner a greater or less portion of the surface soil becomes a nutrient medium, in which an immense culture is developed from which new cases can become infected. A warm climate is more favorable for the unlimited reproduction of the bacillus in the soil than northern countries; hence the greater prevalence of this disease in the tropics.

Infection-Atrium.—As the bacillus of tetanus is the essential cause of the disease, the remaining causes are accidental conditions, which result in the formation of an infection-atrium. *We have no evidence that the bacillus can enter the tissues through an intact mucous membrane or unbroken skin.* Idiopathic tetanus, so called, is a clinical form of tetanus where even the most thorough examination reveals no infection-atrium. As in cases of erysipelas, under similar circumstances, the local lesion may have been so insignificant as not to have attracted the patient's attention, or if he was cognizant of it at the time it may have completely disappeared at the time the first symptoms developed themselves.

In *trismus sive tetanus neonatorum* infection undoubtedly takes place through the umbilicus. In a case of this kind Beumer found the tetanus bacillus in the tissues. There is hardly an operation, capital and minor, which has not furnished its quota to the long list of tetanic patients. It has been observed most frequently after amputation, castration, and extirpation of the thyroid gland.

Weiss reported 13 cases of tetanus occurring after extirpation of the thyroid gland. He attributes the frequency with which this disease follows the removal of this organ to irritation of peripheral nerves induced by the numerous ligatures. Middeldorpf observed paralysis of the facial nerve in some of these cases,—a circumstance which would indicate a central origin of the disease. In 53 total extirpations of the thyroid gland for goitre made by Billroth, tetanus followed in 12 cases, while no cases occurred in 109 partial operations. Two cases became chronic, in which the disease, at the time von Eiselsberg made the report, had lasted for six and nine years. In 7 cases there was, besides the ordinary characteristic symptoms, an involvement of the muscles of the face, neck, larynx, diaphragm, and abdomen; so that dyspnœa and even loss of consciousness occurred. In the fatal cases death occurred in from three to thirty days, and in 1 case after seven months.

Quite a number of cases have been reported during the last few years where it occurred after abdominal section. Tetanus occurring after an operation must be the result of infection through the operation wound with the specific bacillus, which, without exception, takes place by contact. As the bacillus of tetanus is not a pyogenic microbe, it is not necessary that a wound through which infection has occurred should suppurate. When suppuration takes place it is in consequence of a mixed infection. It is a well-known clinical fact that punctured, lacerated, and gunshot wounds of the hands and feet are most liable to be followed by tetanus. Before it was known that tetanus is a microbic disease, the frequency with which this disease complicated such injuries was explained upon the ground that the part injured was abundantly supplied with sensitive nerves, and that the irritation caused by the injury provoked the disease. As thousands of operations upon the hands and feet performed under antiseptic precautions have not resulted in a single instance in tetanus, this explanation is no longer tenable. The antiseptic treatment of wounds has greatly diminished the frequency of tetanus as a complication of operation wounds. Experience has shown that the same treatment which prevents suppuration and other wound-infective diseases has also diminished the frequency of tetanus. Wounds of the hands and feet are so often followed by tetanus, because, in the first place, the implement or substance which inflicts the wound is frequently contaminated with infected earth or dust, and, in the second place, such wounds are often neglected and exposed to subsequent infection from the same sources; and, lastly, infected foreign bodies are often allowed to remain in the wound. In a number of instances animals were successfully infected by inserting under the skin particles of foreign bodies removed from tetanic patients. *Wounds of the hands and feet are no more liable to cause tetanus than wounds in any other part of the body, provided they are not exposed to greater risk of infection.* Infection through the uterus after abortion and during childbed has been repeatedly observed.

Gautier has collected 74 cases of tetanus, 36 following abortion and 38 following confinement. Autopsies were made in 15 cases; 3 presented, on microscopical examination of the brain and cord, no appreciable lesion; in 1 case a retained putrefied placenta was found in the uterus; in 5 suppurative metritis or salpingitis; in 1 ovarian cyst. The other autopsies showed hyperæmia of brain, cord, and meningitis; in 1 hæmorrhage into the lateral ventricles. Ten patients recovered,—5 after abortion, 5 after labor.

Frost gangrene is especially prone to be followed by tetanus. Of 375 cases of tetanus collected by Thamhayn, the disease followed wounds of the fingers and hand in 27 per cent.; of the thigh and leg, 25 per cent.; of the toes and foot, 22 per cent.; of the head, face, and neck, 11 per cent.; of the arm and forearm, 8 per cent.; and of the trunk, 6 per cent. Of 700 cases collected by the same author, the disease was known to have followed a trauma in 603. As males are more frequently exposed to injury than females, the disease is correspondingly more frequent in that sex. The largest number of tetanic patients are found among persons from 10 to 30 years of age, although no age is entirely exempt. According to Larrey, Cullen, and Dupuytren, the disease can be caused, and is always aggravated, by drafts of cold air. That the disease is never caused by exposure to cold requires no argument; that drafts of cold air aggravate the disease when it exists is unquestionable, as every peripheral irritation cannot fail in aggravating the muscular spasms.

SYMPTOMS AND DIAGNOSIS.

The ptomaines of the bacillus of tetanus act upon the brain and spinal cord in a somewhat similar manner as strychnia. If the spinal cord is injured strychnia acts only upon the parts supplied with nerves from the intact portion of the cord. If the posterior roots of the spinal nerves are divided it produces no spasms in toxic doses. If in an animal the brain and medulla oblongata are removed the effect of strychnia upon the muscles is not impaired. Injection of hydrate of chloral arrests the spasm produced by strychnia, and, consequently, chloral must be considered as the most efficient antidote to strychnia. Even the most acute cases of tetanus begin insidiously. The patient, perhaps, complains of a sensation of chilliness and a feeling of soreness about the region of the neck, and shooting pains and stiffness in particular muscular groups. The first symptom which announces the onset of this dreadful disease is difficulty in mastication. The patient discovers, accidentally, that he is unable to open the mouth sufficiently to drink or grasp the food. On inspection nothing abnormal is found, but on trying to separate the teeth the masseter muscle on each side becomes rigid and prominent. This spasm of the muscles of mastication is called *trismus*. It is the first group of muscles affected by the central lesion produced by the ptomaines of the tetanus bacillus. If other causes of this condition, such as inflammatory lesions in the pharynx and the alveoli of the maxillary bones, can be excluded, the existence of trismus is almost a pathognomonic symptom of tetanus. The patient next complains of difficulty in swallowing, as the muscles of deglutition become affected. The next muscular groups to become involved are the muscles back of the neck and the extensors of the spine, giving rise to retraction and fixation of the head and overextension of the spine,—conditions which, when well developed, produce what is called *opisthotonus*. In well-marked opisthotonus the body rests on the occiput and heels when the patient is in the dorsal position. If the body is bent in an opposite direction, from contraction and rigidity of the anterior pectoral and abdominal muscles, the condition is called *emprosthotonus*. Contraction of muscles on the side of the chest and abdomen gives rise to *pleurosthotonus*. *Orthotonus* means tonic spasm and rigidity of all the voluntary muscles,—a condition frequently present in advanced cases of tetanus. The face of tetanic patients presents a characteristic mask-like appearance from the contraction and rigidity of the facial muscles. The muscular spasms are clonic, and are always aggravated by the slightest causes, as walking in the room; touching the bed-clothes or the body of the patient; drafts of air; sudden, unexpected noises. The affected muscles are rigid from tonic contraction, but this state of rigidity is increased by the paroxysmal clonic spasms.

In acute cases the temperature soon rises to 40° to 41° C., and the pulse is correspondingly increased in frequency. The temperature curve shows but little change during twenty-four hours. The sensorium usually remains unaffected throughout the entire course of the disease. As the patient finds it difficult to clear the mouth, the profuse salivary secretion escapes from the mouth. Respiration is impeded in proportion to the number of the respiratory muscles affected. In severe cases early dyspnœa and cyanosis are present. Special senses remain intact. The pain is mostly excruciating, extending from the neck and back in the direction of the nerves, leading to the affected muscular groups. The pain is always aggravated with the increased convulsive movements, resulting from the action of external irritants.

In consequence of deficient food-supply, the intense pain, and loss of sleep, rapid emaciation and loss of strength appear as early and constant symptoms. Approaching exhaustion is announced by profuse clammy perspiration, coldness of the extremities, and a rapid, feeble, and intermittent pulse. As soon as the intercostal muscles are affected respiration becomes more and more embarrassed, and when finally the diaphragm is thrown into a tonic spasm respirations and pulse cease, general cyanosis follows, and death may ensue during the first spasm of the diaphragm. Should, however, the patient rally from this attack, he will be almost certain to succumb to the second or third attack.

Wunderlich has seen the temperature shortly before death rise to 42° or 43° C., and the same has been observed in animals dying from tetanus by Billroth, Fick, and Leyden. A post-mortem rise in temperaure to 44.7° C. has been recorded by Wunderlich, and he attributed this trange phenomenon to paralysis of the central heat-moderators. In hronic tetanus the disease commences very insidiously, and the graver ymptoms, such as a very high temperature, feeble and intermittent pulse, spasm of the intercostal muscle and diaphragm, are absent. The temperature is normal or only slightly elevated. Trismus is always present, to which may be added spasm and rigidity of the muscles of the back of the neck and the extensors of the spine. The trismus makes it difficult to administer food in sufficient quantity, and, on this account, progressive emaciation is one of the prominent features of this form of tetanus, as the disease, as a rule, lasts from six to ten weeks. The disappearance of symptoms is as gradual as their onset. In the differential diagnosis it is important to distinguish between tetanus and strychnia poisoning, hysteria, catalepsy, hydrophobia, cerebro-spinal meningitis, and basilar meningitis. With few exceptions it is possible in tetanus to establish the fact of infection, and the clinical history shows that different muscular groups become involved successively in regular order, first trismus, then rigidity of the muscles at the back of the neck, and, finally, opisthotonus. In acute cases the disease is attended by a continuously high temperature. In strychnia poisoning the maximum symptoms, opisthotonus or orthotonus, are developed suddenly, as soon as a toxic dose of the drug has been absorbed. The convulsive movements in hysteria are not limited to any definite muscular groups, and the pulse and temperature are normal. The same can be said of catalepsy. In hydrophobia, as we shall see subsequently, the spasms are limited to the muscles of deglutition, the stage of incubation is longer than in tetanus, and infection is always caused by the bite of a rabid animal, usually a dog. In cerebro-spinal meningitis muscular spasm and rigidity are limited to the extensor muscles of the spine; so that, even if the disease has caused well-marked opisthotonus, trismus is absent. Tubercular meningitis is usually ushered in by intense headache, vomiting, and photophobia, and if tonic muscular spasms set in they affect the muscles at the back of the neck almost exclusively. Trismus is never present.

CLINICAL FORMS OF TETANUS.

Acute Tetanus.—The stage of incubation, as a rule, is shorter than is the chronic form of the disease. Trismus develops gradually, but after it has once been established the extension of the disease to other muscular groups is rapid. A high temperature and rapid, feeble pulse are always present. Respiration is mechanically embarrassed by the successive implication of the different muscular groups which are concerned in the function of respiration, the last one to become affected being the diaphragm. The disease may prove fatal in twenty-four hours, and the duration is seldom prolonged for more than a week.

Chronic Tetanus.—The disease not only commences insidiously, but the symptoms appear gradually and never develop to the same extent as in acute tetanus. The most marked feature is trismus, which may be followed by a mild degree of opisthotonus. The muscles of respiration are not implicated, and if death result it is from marasmus and exhaustion and not from apnœa. The duration of the disease is seldom less than six, nor more than ten, weeks.

Trismus.—Tetanus in which only the muscles of mastication are affected is called trismus. With the exception of the infantile form, trismus is a chronic and comparatively benign affection.

Tetanus Neonatorum.—Tetanus occurring in infants during the first week after birth is clinically characterized as trismus, and proves fatal almost without exception in a few days. Infection takes place through the umbilicus before or after separation of the cord. It is a disease that occurs much more frequently in tropical than northern climates, for reasons which have been heretofore explained.

Tetanus Hydrophobicus, or Head Tetanus.—This is a form of tetanus which was first described by E. Rose, in 1870. In the cases which have been reported, it followed head injuries, especially wounds of the face. Besides trismus, it is characterized by paralysis of the facial nerve on the injured side. During deglutition, the muscles which are concerned in this act are thrown into spasm, and on this account the disease bears a strong resemblance to hydrophobia. Klemm has collected up to date 24 reported cases of this disease. Most of them recovered, and in those that died the disease passed into the typhoid form of tetanus.

PROGNOSIS.

The most important element in prognosis is the type of the disease. The more acute the onset and the more intense the symptoms, the greater the immediate danger to life. If death does not occur within two weeks the prospects of an ultimate recovery are good. Of 280 cases which comprise the Calcutta statistics of this disease 75 per cent. proved fatal. This list represents about the average mortality of this disease. The greater the excitability of the motor centres of the spinal cord, and the more rapid the successive involvement of different muscular groups, the greater the danger of an early dissolution. In acute cases death is always preceded by great dyspnœa, and death usually occurs during an attack of convulsions, in which the intercostal muscles and the diaphragm take part. Chronic cases terminate, as a rule, in recovery after an illness lasting from six to ten weeks.

PATHOLOGY AND MORBID ANATOMY.

The absence of gross pathological changes is characteristic of tetanus. The only constant lesion found is a hyperæmic condition of the medulla oblongata and the spinal cord, to which special attention has been called by Leyden, Joffrey, Ranvier, and Robin. As all of the peripheral manifestations of the central lesion point to an increased excitability of the nervous centre, we would expect that the principal lesions are to be found in the gray substance of the cord. In 1857 Rokitansky described tetanus as an ascending neuritis. He found a connective-tissue proliferation, in the form of a semi-fluid, adhesive, grayish substance, between the medullary elements of the nerves leading from the infected district. In some cases he found extensive destruction of the nerve-tubes, and their space occupied by the products of granular degeneration,—colloid and amyloid corpuscles.

Lockhart-Clark and Dickinson found, as the most constant pathological lesion, inflammatory softening of the gray substance of the cord and dilatation of the vessels. Michaud and Benedict found cell proliferation into the anterior cornua of the cord and great vascularity. Elischer regarded the central lesion as a myelitis with vacuolation in the ganglia-cells. Tyson found in 2 cases destruction of the central canal of the cord, with disintegration of the posterior cornua. Aufrecht narrowed the morbid anatomy of tetanus down to atrophy of the anterior horns, in the cervical portion of the spinal cord. Schultze was never able to discover any evidences of myelitis. The hyperæmia of the cord, which is so constantly found, may be the result of a passive congestion; at present this cannot be accepted as proof of inflammation, because in most cases the anatomical and clinical evidences do not sustain this supposition. The view that tetanus is essentially an ascending neuritis, as was claimed by Rokitansky, is no longer tenable, since it is not supported by the results of recent investigations. It is left for future research to furnish more reliable information concerning the pathology and morbid anatomy of tetanus. At present we can only surmise that the ptomaines of the bacillus act upon the gray matter of the cord, where minute lesions are produced, which must account for the clinical manifestations of the disease.

TREATMENT.

The prophylactic treatment of tetanus has in view the prevention of infection by the usual antiseptic precautions in the treatment of wounds and local lesions which might become the necessary infection-atrium. As tetanus follows more frequently injuries insignificant in themselves than large wounds or major operations, it behooves the surgeon to treat the minutest lesions with the greatest care, and in strict accordance with antiseptic principles. Foreign bodies should be carefully searched for and removed. Even the most recent accidental wounds should be treated as infected wounds, and should be rendered aseptic by a thorough primary disinfection. The antiseptic treatment must be continued until the wound is completely healed, and during this time the injured part must be kept at rest. Wounds of the lower extremities must be treated by confining the patient to bed, and wounds of the upper extremities demand, in their treatment, fixation of the limb upon some kind of a splint or, at least, suspension in a sling.

In acute cases of tetanus the most that can be expected from treatment is palliation. The excruciating pain is often only relieved by inhalation of chloroform. The administration of chloroform should be conducted by the physician in attendance or a reliable assistant, and should only be carried to the extent of relaxing the contracted muscles, and repeated as often as necessary to procure rest. Morphia in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain, with $\frac{1}{200}$ grain of atropia, should be given hypodermatically every three or four hours until the desired effect is reached. In less severe cases the internal use of hydrate of chloral and potassic bromide, each in doses of from 15 to 20 grains, can be given every three or four hours with excellent effect. Woorara, which has been quite extensively used in the treatment of the disease, is absolutely contra-indicated, as its paralytic effect on the heart cannot fail in producing anything but a deleterious effect.

All patients suffering from tetanus should be kept in a quiet, dark room, and all kinds of excitement must be carefully avoided, as bodily and mental rest are important elements in the treatment. As mastication is impossible, the patient must be nourished with liquid food, which he can sip through an elastic tube. If swallowing is impossible, a small elastic tube is introduced through one of the nostrils into the stomach, and food is administered at regular intervals by this method. In chronic tetanus warm baths are grateful to the patient, and exercise a decided influence in ameliorating the symptoms. The surgical treatment of tetanus has yielded no better results than the internal use of drugs. In all cases the infection-atrium should be carefully examined, and, if necessary, the wound or local lesion should be thoroughly disinfected, as this treatment may be the means of preventing further infection from this source. Scars should be excised and foreign bodies removed.

Under the belief that tetanus is an ascending neuritis, nerve-section, or neurotomy, has been practiced for the purpose of preventing further extension of the inflammation by interrupting the continuity of the nerve; but the results, as could be expected, were disappointing, and the operation has fallen into well-deserved desuetude. When nerve-stretching

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coveries in all cases of tetanus not treated by surgical resources.
tation is only indicated in cases where the local conditions which
rise to tetanus make it necessary to resort to this operation.

CHAPTER XVI.

HYDROPHOBIA.

HYDROPHOBIA, lyssa, canine madness, and rabies are synonymous terms used to designate a nervous disease caused by the bite of a rabid dog or other animal, attended with violent spasms if the patient attempts to swallow water or other liquids, and by embarrassment of respiration from spasm of the laryngeal muscles. This disease never occurs spontaneously in man, but is always the result of inoculations with the virus of a rabid animal. Although this disease never originates elsewhere than in the dog and animals belonging to the same species, the wolf, fox, and jackal, the virus of rabies is capable of being communicated to all warm-blooded animals. It has been estimated that in man the disease is derived in nine out of ten cases from dogs; sometimes it is contracted from cats, and sometimes, but very rarely, from foxes or wolves. The specific virus of hydrophobia appears to be generated in the glandular appendages of the mucous membrane of the mouth and throat, and is transmitted by the saliva of the rabid animal. For this reason it has been observed that inoculation is more apt to take place from a bite on an uncovered part of the body, as, for example, on the hands or face, than from a bite inflicted through the clothes, as in the latter case the greater portion of the saliva is deposited in the clothing. Not every person bitten by a rabid dog necessarily contracts the disease, as statistics have shown that about one-third of the animals and human beings bitten by mad dogs escape all danger. This partial immunity is explained in part by the virus being diluted, and being wiped from the teeth of the rabid animal by clothing; and also by well-ascertained facts proving the absence of susceptibility to its action in certain individuals, both in animals and in man.

Renault's careful experiments proved that one-fourth of the inoculated creatures escaped the effects of the inoculations, which were mortal in the other three-fourths. As in civilized countries the disease is contracted almost exclusively from rabid dogs, it is necessary to call attention to the symptoms which characterize the disease in this animal, in order that it may be recognized in time, so that the infected animal can be isolated and kept in close confinement until the result shall prove or disprove the correctness of the diagnosis. It is a great mistake to kill an animal suspected to be rabid, until by careful observation continued for some length of time, or from the result of the disease, a positive diagnosis can be made, and thus a great deal of unnecessary fear may be avoided.

HYDROPHOBIA IN THE DOG.

The name "hydrophobia," meaning literally a dread of fluids, is a proper designation for the disease as it occurs in man, because a peculiar dread of fluids is the most characteristic symptom of this disease in the human being. This symptom does not exist in the dog; hence, in this animal we should speak of the disease as rabies, in man as hydrophobia. Fleming, who is an acknowledged authority on everything that pertains to hydrophobia, makes the following statement in reference to the ability of rabid animals to take fluids: "The many hundreds of rabid dogs seen by Blaine, Youatt, and others did not evince any marked aversion to fluids. On the contrary, the rabid animal is generally thirsty, and if water be offered will lap it up with avidity, and, at the commencement of the disease, will always swallow it. When, at a later period, the constriction about the throat, which is symptomatic of the malady, renders swallowing difficult, the animal does not the less endeavor to drink, and lappings are as frequent and prolonged as deglutition is retarded. Even then we see the suffering creature, in despair, plunge its entire muzzle into the vessel, and gulp at the water as if determined to overcome the spasmodic closure of the throat by forcing down the fluid. Tantalus did not experience a greater torment with regard to water than does the unlucky dog." The excessive sensibility to pain and the action of the mildest external irritants so characteristic of hydrophobia in the human being are absent in the rabid dog. The animal is almost insensible to pain; he will dash himself against the bars of his kennel, tear them when his mouth is lacerated and bleeding, and he has been known to seize a red-hot poker in his mouth and hold on to it, apparently unconscious of suffering. Rabies in the dog must be suspected when the animal becomes dull, morose, mopes, and avoids his master and companions. During the commencement of the disease the animal is exceedingly restless, and is always on the move, prowling, snapping, and barking at imaginary objects. During the first two or three days there is rarely any tendency on the part of the animal to bite, nor to paroxysms of uncontrollable fury.

The danger in this stage to man and other animals comes from licking rather than biting, for there is a propensity to extraordinary demonstrations of affection. After a time, however, a paroxysm of maniacal fury comes on, generally provoked by the sight of another dog. When this has subsided the animal again becomes controllable, but manifests a strange disposition to wander from place to place. He is now most dangerous. With a slinking and troubled aspect, his head and tail down, his eyes suffused, and foam at his mouth, he walks or trots along, snapping and biting at real and imaginary objects. He is only aggressive when attacked, and then his fury seems unbounded. When tired out from inadequate nourishment and the ceaseless wanderings, he drops exhausted in some out-of-the-way, solitary corner, and, after a rest, starts off again on his lonely journey, seemingly impelled by some irresistible force, and is finally killed or dies of exhaustion. The duration of the disease in the dog never exceeds ten days, and in the majority of cases the animal dies on the fourth or the sixth day after the appearance of the first symptoms. From a study of the symptoms in this animal we can readily distinguish three stages: 1. Prodromal. 2. Irritation. 3. Paralytic.

During the prodromal stage the most noticeable changes refer to the altered habits of the animal, while the stage of irritation culminates in attacks of ungovernable rage, provoked by real or fancied causes. The last, or paralytic, stage precedes death, which takes place from exhaustion. The period of incubation in the dog is variable; it is usually from six to twelve weeks, but may extend to a much longer period. Frank, from a study of 200 observed cases of rabies in the dog, found that the average period of incubation was three months; the extremes, six and seven days, and eleven months.

HYDROPHOBIA A MICROBIC DISEASE.

Raynaud and Lannelongue discovered that rabbits could be successfully inoculated with saliva from rabid animals. Pasteur corroborated these observations by his own experiments, and cultivated from the blood of the infected rabbits in veal-bouillon a micro-organism which in its shape resembled the figure "**8**"; this microbe was surrounded by an envelope of a gelatinous substance. In the cultures these rods are said to have become converted into chain cocci. Fowls and guinea-pigs were not found susceptible to inoculations with cultures of this microbe. After Pasteur had regarded these micro-organisms as the cause of hydrophobia, he produced the same disease in rabbits by inoculations with saliva from healthy persons. Vulpian also succeeded in producing, by inoculations of normal saliva in rabbits, a disease which proved fatal in two days; and with a small quantity of blood taken from the dead animals the disease could be communicated to other rabbits. The disease thus produced was probably the same as that described by Sternberg. This observer caused marked septicæmia in rabbits by injecting subcutaneously his own saliva in small doses. Injections of 1.25 to 1.75

cubic centimetres, with few exceptions, caused death, usually within forty-eight hours. The constant and characteristic lesion found was a diffuse cellulitis, or inflammatory œdema, extending in all directions from the point of injection, attended with an abundant exudation of bloody serum, swarming with micrococci. Hæmorrhagic extravasations in the connective tissue, and in various organs, were of frequent occurrence, and changes in the liver and spleen, such as are common in rapidly-fatal septic diseases, were generally found. The disease could be communicated by dipping a hypodermic needle into the blood of a rabbit just dead from the result of an injection of saliva; inoculating a healthy rabbit, a rapidly-fatal septicæmia was produced.

Gibier found, in the brain of hydrophobic animals, round, shining granules, which stained slowly and imperfectly in aniline dyes.

Fol stained the brain-substance, according to Weigert's method, and discovered in the hollow spaces of the neuroglia groups of micrococci. The same microbe he found also in the nerve-fibres, between the sheath and axis-cylinder. Babés stained the specimens according to Gram's method, and found cocci in the cells, especially those of the surface of the brain. The cocci looked like diplococci, and were always found aggregated in flat clusters. Fol and Babés claim to have succeeded in obtaining a culture of the microbes found in the brain. The former used for nutrient medium a filtrate of triturated brain and parenchyma of salivary gland. Of 8 dogs, rats, and rabbits inoculated with the first culture, 5 died of well-marked hydrophobia; of 8 dogs inoculated with the second culture, four died. The inoculations were always made by infecting the brain through an opening in the skull. The microbes in the cultures corresponded in shape and size with those found in the brain of hydrophobic animals. The third series of cultures produced only negative results. The microbes in these cultures were more readily stained than most of the first two cultures. Babés cultivated the microbe upon gelatin and coagulated blood-serum, to which was added brain-substance obtained from rabbits. The cultures grew slowly, and appeared as gray spots. Successful inoculations were made with the second and third generations.

The microbe of hydrophobia exists, but so far it has not been discovered. That hydrophobia is a microbic disease can no longer be doubted. At the present time we can safely assert, without fear of contradiction, that the essential cause of this disease is a specific virus, which can only be reproduced within the living organism. As a small quantity of this virus introduced into the tissues can result in the most serious consequences, there exists no doubt that it possesses the properties pertaining to living organisms, more especially the capacity of reproduction after its entrance into the body. That the disease is not caused by preformed ptomaines, communicated from the saliva of rabid animals, is shown by the variable and, on the whole, long stage of incubation which precedes all true infective processes. Another convincing proof of its microbic origin is the well-established fact that the disease can be artificially produced by implanting fragments of brain- or cord- tissue, taken from animals dead of rabies, into healthy animals. Furthermore, the blood and secretions of a rabid animal, its flesh and viscera, even the cooked flesh of a rabid ox, when eaten, would seem to be capable of conveying the disease. A pupil at the veterinary school of Copenhagen inoculated himself with the virus by cutting his finger slightly, while examining the body of a dog that had died of rabies on the evening before; the student died of hydrophobia in six weeks. The clinical symptoms, as well as the pathological conditions found in the brain and spinal cord of hydrophobic patients, bear such a strong resemblance to tetanus that it appears probable that the microbe possesses analogous pathogenic properties, and that the actual development of the disease follows the action of its ptomaines upon the central nervous system. The latent stage of the disease, or the long duration of the period of incubation, depends either upon the slow growth of the microbes or that these reach the place slowly from where they exert their specific pathogenic properties.

CAUSES.

The microbe of hydrophobia does not penetrate the intact skin or healthy mucous membrane; hence its entrance into the tissues takes place through an infection-atrium, usually a punctured wound made by the bite of a rabid animal. As the microbe pre-exists in the saliva of the rabid animal, inoculation takes place at the time the wound is inflicted. Infection, however, can take place by the deposition of the infected saliva upon a surface from which absorption can take place. This can occur from the licking of a wound or abraded surface by an infected dog, as happened in one of my cases. A lady of rank and fashion had a pimple on her face, from which she had scratched off the head. Hydrophobia was thus contracted, and she perished by this terrible disease.

SYMPTOMS AND DIAGNOSIS.

Great diversity of opinion exists as to the length of the period of incubation in man. In the 2 cases of hydrophobia that have come under my own observation, the time of infection and the onset of the disease could be accurately fixed, and in both of them *the stage of incubation lasted forty-two days.* In 106 cases of hydrophobia in human beings of all ages, collected by Bonley, 23 occurred within two months after infection, and the remainder came in at varying periods, the longest time noted being eight months. The cases reported where it was supposed the disease developed some years after the persons were bitten by a dog lack accuracy of observation, and either the diagnosis was not correct or infection occurred more recently, as we have the authority of Fleming that the disease never occurs later than eight months after inoculation. Age appears to have some influence in modifying the duration of the stage of incubation. In the cases where the length of this stage could be accurately ascertained, in patients under 20 years of age the mean period of incubation was six weeks; from 20 up to 72 it was two months and a half. Before the actual development of the disease in man, there is usually a period of a few days during which ill-defined premonitory symptoms can be detected The wound through which the virus entered is the seat of a sensation of uneasiness and itching, and sometimes of actual pain, which radiates along the course of the nerves of a limb. The cicatrix often presents a congested appearance, and is tender on pressure. The patient is melancholic and irritable, and sleep is disturbed. The first characteristic symptom of hydrophobia in man is a sense of tightness and choking about the pharynx, attended by a hesitation in swallowing, especially of liquids. In one of my cases this early disturbance of the function of the muscles of deglutition made it possible for me to recognize the disease a few hours after the attack commenced. The patient was a sailor, about 30 years of age, who sent for me to treat him for a supposed cold. The only thing he complained of was a sense of constriction in the throat and difficulty in swallowing. In examining the cavity of the mouth and pharynx for evidences which would explain the existing symptoms, I found a profuse salivary secretion; the mucous membrane of the pharynx was congested, but no signs of deep-seated inflammation could be found in the region of the tonsils. My suspicions were awakened at once. I ascertained that six weeks before a small pet dog owned by the family had died after a few days of illness, and that one day during this time, when the patient was lying on his back on the floor, the dog had licked a small sore on the anterior surface of the lobe of the left ear. Requesting the patient to drink water from a glass which I handed him, I noticed a hesitation on his part to comply with my wish; but finally he grasped the glass with both hands, which trembled considerably, and, after waiting for the proper moment to come, applied it rapidly to his lips and made a desperate but futile effort to swallow; the attempt was repeated several times, but only a very small amount was swallowed. The next group of muscles to become affected with convulsive spasms are the muscles of respiration about the larynx. The symptoms of a well-developed case of hydrophobia are so well depicted by Fleming that I will give his own description. "The difficulty in swallowing rapidly increases, and it is not long before the act becomes impossible, unless it is attempted with determination, though even then it excites the most painful spasms in the back of the throat, with other indescribable sensations, all of which appal the patient and cause him to dread the very thought of liquids. Singular nervous paroxysms or tremblings become manifest, and sensations of stricture and oppression are felt about the throat and chest. The breathing is painful and embarrassed, and interrupted with frequent sighs or a peculiar kind of sobbing movement, or catching of the breath; there is a sensation of impending suffocation and of necessity for fresh air. Indeed, the most marked symptoms consist in a horribly violent convulsion or spasm of the muscles of the larynx and pharynx, or gullet, by which swallowing is prevented, and at the same time the entrance of air into the windpipe is greatly retarded. Shuddering tremors, sometimes amounting to general convulsions, run through the whole frame, and a fearful expression of anxiety, terror, and despair is depicted on the countenance."

Frothing at the mouth is rarely observed, but the viscid, tenacious mucus in the fauces and the profuse salivary secretion are frequently forcibly ejected by hawking and spitting. Shortly before death the patient's mouth is often full of this mucus or froth, which in some cases is tinged with blood. The pulse at first is not much changed in force and frequency, but as the disease advances it becomes feeble and rapid, and often intermittent. The temperature is always increased. In both of my cases the thermometer registered from 101° to 103° F. at different times in the axilla. A post-mortem temperature of 106.2° F., taken in the rectum immediately after death, has been recorded.

Occasionally the patient has hallucinations of sight and hearing, but usually the mental faculties are not much impaired. One patient, alluded to by Trousseau, heard the ringing of bells, and some mice run about on his bed. To the by-stander the most distressing phenomenon presented by hydrophobic patients is the fear of impending death, which is usually manifested soon after the attack, and remains throughout the whole course of the disease. No kinds of assurances or consolation are able to dispel it. Death occurs from complete exhaustion, in most cases attended by well-marked evidences of asphyxia from spasm of the glottis; sometimes a convulsion is the final symptom, as in tetanus.

The differential diagnosis between hydrophobia and tetanus is not always easy. In both diseases the stage of incubation is variable, and both are characterized by excessive excitability of the cerebro-spinal centre, as is evident from the muscular spasms and great hyperæsthesia of the entire surface of the body during the stage of irritation. In hydrophobia infection always takes place from the bite of a rabid animal, and the difficulty in swallowing is not caused by spasm of the pharyngeal muscles, but by tonic contraction of the muscles of mastication, notably the masseters. In tetanus respiration is impaired by rigidity of the respiratory muscles of the chest; in hydrophobia by spasmodic contractions of the respiratory muscles of the larynx. Acute softening of the brain, and meningitis affecting the base of the brain and upper portion of the spinal cord, may give rise to symptoms that bear a faint resemblance to the clinical picture of hydrophobia, but a careful study of the symptoms, individually and collectively, will disclose the real nature of the case under consideration. A purely neurotic affection has been described as *lyssa nervosa falsa*, which, it has been said, resembles genuine hydrophobia closely. Such cases are undoubtedly one of the manifold manifestations of hysteria; and, if so, it can be differentiated from true hydrophobia by the absence of fever and by the fact that the muscular spasms are not limited to the muscles of deglutition and the muscles of the larynx. Trousseau speaks of *lyssa nervosa falsa* as a mental hydrophobia. Fayrer describes a case of this kind in a young Scotchman in India, and Böllinger quotes a case of a boy who was twice frightened into simulated hydrophobia.

In making a positive final diagnosis of hydrophobia, it is necessary to establish, in the first place, the fact that infection occurred from a rabid animal within eight months from the development of the disease; and, in the second place, it is necessary to prove the existence of spasms of the muscles of deglutition in attempts to swallow liquids; and if at the same time spasms of the muscles of the larynx interfere with the function of respiration, all doubt as to the nature of the difficulty has been removed.

PROGNOSIS.

If any doubt existed as to the nature of the case during life, an early fatal termination will corroborate the suspicions that may have been entertained. Décroix reports 9 cases of spontaneous recovery in dogs. *In man this terrible disease is invariably fatal; there is no authentic instance on record of recovery from genuine hydrophobia.* Death results unexpectedly, suddenly, or from apoplexy, asphyxia, or exhaustion, in from twelve hours to six days from the appearance of the first symptoms. The mean duration of the disease is about four days One of my patients died on the fourth and the other on the fifth day after the attack. In 90 cases collected by Bonley, death occurred in 74 during the first four days, the largest proportion of these being on the second and third days. In only 16 was life prolonged beyond the fourth day.

PATHOLOGY AND MORBID ANATOMY.

Hydrophobia, like tetanus, to which disease it is so closely allied in many respects, is characterized by the absence of gross pathological changes in the nervous centres and at the primary seat of infection. The scar which marks the wound or lesions through which infection occurred may be red and slightly swollen, but these changes are not present in all cases. Hydrophobia is a disease in which there is every indication of irritation of certain nerve-centres and of a greatly increased reflex irritability. The centres irritated here are less those of the cerebral hemispheres than of the spinal cord and medulla oblongata. The symptoms point mainly to the medulla oblongata, and after death well-defined vascular lesions can be detected in this structure by means of the microscope.

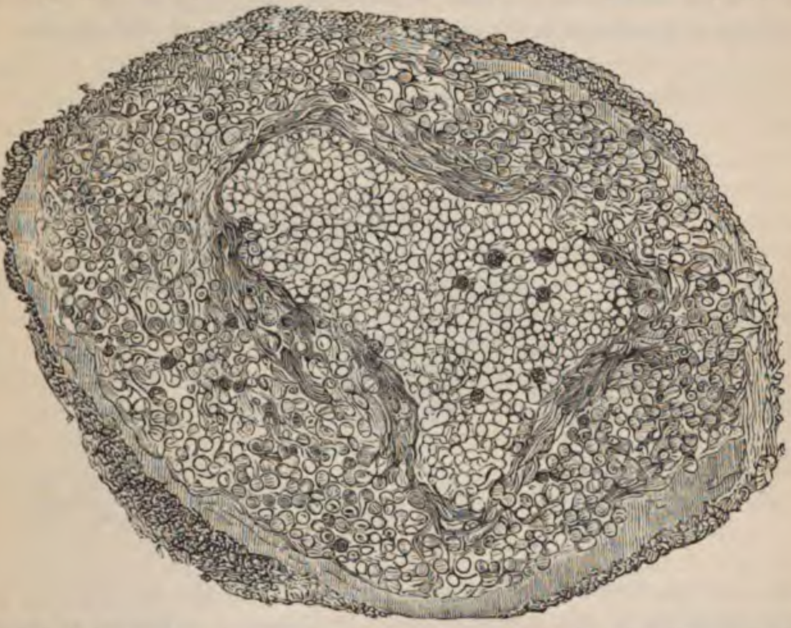

FIG. 90.—A BLOOD-VESSEL FROM MEDULLA OBLONGATA IN A CASE OF HYDROPHOBIA. LARGE NUMBERS OF ROUND CELLS ARE SEEN IN ITS SHEATH. ×350. (*Coates.*)

Similar lesions, but less marked, can be found in the spinal cord, and still to a lesser degree in the other parts of the nervous system. The most prominent condition is an accumulation of leucocytes around the vessels in the substance of the cord and medulla oblongata. Where the local lesion is most advanced the vessels are surrounded by several layers of leucocytes, which would indicate that the microbe of hydrophobia or its ptomaines produce an alteration of the capillary wall of sufficient intensity to entitle the process to be called inflammation. An increase of leucocytes is evident everywhere, so much so that the collections which can be found in different parts have been called miliary abscesses. As the leucocytes show no evidences of even approaching transformation into pus-corpuscles, these aggregations of leucocytes do not deserve the name of abscesses. Klebs is of the opinion that the microbe of hydrophobia does not enter the circulation directly, but invades in preference the lymphatic vessels, as he found general lymphatic engorgement in a recent case. The same author also discovered, particularly in the submaxillary gland, deposits of finely granular, strongly refractive corpuscles of a faint, brownish color, closely packed together in clusters and rows, which he regards as possibly the vehicles for the transportation of the specific virus. Well-marked evidences of leucocytes have been found by many in the salivary glands.

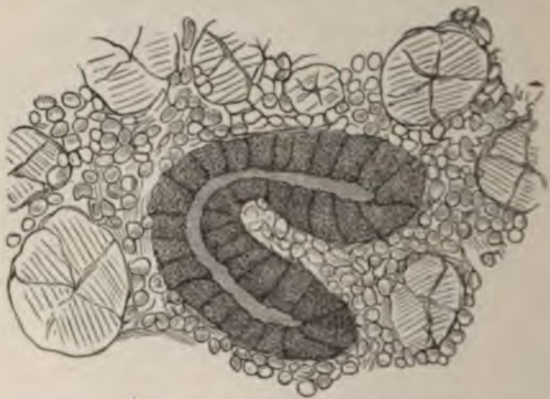

FIG. 91.—FROM THE SALIVARY GLAND IN A CASE OF HYDROPHOBIA. IN THE MIDDLE IS THE PORTION OF A DUCT; ABUNDANT ROUND CELLS AROUND IT AS WELL AS THE GLANDULAR STRUCTURES SHOWN IN OUTLINE. ×350. (*Coates.*)

There is hyperæmia and œdema of the substance of the brain, medulla oblongata and cord, and of their membranes; deep-red injection of the mucous membrane of the pharynx and epiglotis, and sometimes recent swelling of the tonsils, follicular glands of the tongue, pharyngeal follicles, and of the lymphatic glands in the neighborhood of the jaw. The stomach and intestines show decided injection, and often hæmorrhagic extravasations. The lungs are charged with blood, with frequent points of capillary hæmorrhage, and sometimes emphysema as a result of the dyspnœa. In the kidneys, also, there are signs of irritation in the form of dilatation of vessels and hæmorrhage. According to Bollinger, the anatomical picture bears the strongest resemblance to that seen in cases of death from asphyxia or thirst. The conditions found, post-mortem, furnish an illustration that here an intense irritant is circulating in the blood, and the intensity of it may be judged from the fact that all these very marked appearances, although nearly all of them recognized only by the use of the microscope, occur in the short space of three or four days.

TREATMENT.

As hydrophobia is an absolutely fatal disease, the treatment resolves itself into prophylactic measures to prevent the disease, and means of palliation after it has developed.

Prophylactic Treatment.—The most effective prophylactic measures consist in preventing the spread of the disease, among animals, by the killing or strict isolation of animals which present symptoms of rabies. If animals, which are suspected of being rabid, are known to have bitten persons, they should not be killed at once, but should be kept in close confinement unknown to the injured person, until, by observation or the course of the disease, a positive diagnosis can be made. As soon as a positive diagnosis of rabies can be made, then the animal should be killed to prevent any further possibility of infecting other animals or persons. If a person is bitten by an animal which presents suspicious symptoms, no time should be lost to prevent infection by removing or destroying the virus.

(a) Excision of Wound.—As the virus of hydrophobia appears to be slowly diffused in the tissues, thorough local treatment of the wound may prove successful in preventing infection, even if resorted to several hours or days after inoculation has occurred. As soon as possible after the bite has been inflicted, a constrictor should be applied on the proximal side of the wound and medical aid summoned without delay. In the meantime an attempt should be made to remove the virus from the wound by suction. In recent cases the simplest and safest treatment consists in excising the tissues in the immediate vicinity of the puncture, and after thorough disinfection close the wound with sutures.

(b) Cauterization of Wound.—The same object is accomplished, but with a lesser degree of certainty, by cauterization. The most efficient caustic is the actual cautery. With the knife-point of a Paquelin cautery the wound is deeply cauterized, and the resulting eschar is protected against infection with pus-microbes by an antiseptic dressing. Of the chemical caustics the most valuable are caustic potassa, nitric acid, sulphuric acid, and nitrate of silver, their efficiency being estimated in the order named. The authority for excision and thorough cauterization, as prophylactic measures, is to be found in the fact that, of 134 collected cases, in which bites of mad dogs were cauterized, 68 escaped and 42 died,—a degree of immunity far above the average, which is 33 per cent. (Bonley.)

(c) **Prophylactic Inoculations.**—Pasteur has shown, by a long series of inoculations, made first in monkeys, rabbits, and guinea-pigs, and later exclusively in rabbits, that if the virus of hydrophobia is introduced into the brain of these animals the disease is invariably produced after a fixed period of incubation. As the period of incubation in successive inoculations in the same animal is shortened, we must take it for granted that the virulence of the material is increased. In the rabbit the first inoculation under the dura mater is followed by a period of incubation of fourteen days' duration, which, in successive inoculations in the same animal, is reduced to seven days. Back inoculations in dogs produce in these animals fatal rabies in the same length of time. Pasteur made an additional important discovery, as he found that the spinal cord of the inoculation rabbits, increased in virulence by successive inoculations, is again diminished in its virulence by preserving it in dry air, guarding at the same time against contamination with other micro-organisms. This discovery led to a method by which the virulent action of such preparations can be accurately graded, inasmuch as the action of the spinal cord, in the drying-room, in 7 to 8 days is reduced from its highest degree of virulence to *nil*. By using the spinal cord of rabbits treated in this manner in different strengths, at first weak and then gradually stronger preparations, it was found possible to render animals immune to the action of inoculation material of the highest potency. By this method Pasteur succeeded in creating absolute immunity against the strongest hydrophobic virus in 50 dogs. The success of these prophylactic inoculations in animals enabled Pasteur to resort to the same method of treatment in persons bitten by rabid animals, as the long stage of incubation made it possible to carry out this treatment before the actual development of the disease was expected. The first human being subjected to this treatment was on July 5, 1885, and from that time until the close of the year 1889 2682 persons bitten by rabid animals, or animals that were suspected of being mad, with the result that of this large number only 31 died, equivalent to 1.15 per cent., while the general mortality in persons under similar circumstances without such prophylactic inoculations has been at least 16 per cent. The danger is always greatest when the bite is inflicted by rabid wolves. Pasteur collected 100 cases of persons bitten by rabid wolves, and of this number not less than 82 died. Pasteur had an opportunity to submit to his treatment 38 persons bitten by rabid wolves, and of this number only 3 died,—a mortality of 7.89 per cent.

The following tables represent Pasteur's work for four years:—

YEARS.	TABLE A.			TABLE B.			TABLE C.			TOTAL.		
	Persons Treated.	Died.	Mortality (per cent.)	Persons Treated.	Died.	Mortality (per cent.)	Persons Treated.	Died.	Mortality (per cent.)	Persons Treated.	Died.	Mortality (per cent.)
1886 . .	231	3	1.30	1926	19	0.99	514	3	0.58	2671	25	0.94
1887 . .	357	2	0.56	1156	10	0.86	257	1	0.39	1770	13	0.73
1888 . .	402	6	1.49	972	2	0.21	248	1	0.40	1622	9	0.55
1889 . .	346	2	0.58	1187	2	0.17	297	2	0.67	1830	6	0.33
Total . .	1336	13	0.97	5241	33	0.63	1316	7	0.53	7893	53	0.67

The bites have been divided into three categories,—

1. Those of the head and face;
2. Those of the hands;
3. Those of the limbs and trunk,—with the following result:—

	TABLES A AND B.			TABLE C.			TOTAL.		
	Persons Treated.	Died.	Mortality (per cent.)	Persons Treated.	Died.	Mortality (per cent.)	Persons Treated.	Died.	Mortality (per cent.)
1. Head and face	593	14	2.36	79	1	1.27	672	15	2.23
2. Hands	3768	26	0.69	619	3	0.48	4387	29	0.66
3. Limbs and trunk	2216	6	0.27	618	3	0.48	2834	9	0.32
Total	6577	46	0.70	1316	7	0.53	7893	53	0.67

Table A comprises those persons bitten by animals determined to be rabid by experiments in rabbits, made in the laboratory, or by the death of other animals, or persons, bitten by the same animal.

Table B comprises those persons bitten by animals demonstrated to be rabid by the examination of a veterinary surgeon, or by the clinical signs shown during life.

Table C comprises those persons bitten by animals suspected to be rabid.

These results must convince the most skeptical of the practical utility of Pasteur's prophylactic treatment against hydrophobia, and, although the method will not be perfect until the microbe of this disease is discovered and mitigated (pure cultures are employed), this crude method must be viewed as a great boon to a class of patients otherwise exposed to the risks of contracting the most terrible and hopeless of all diseases. Pasteur institutes have sprung up in different parts of the civilized world, and the accumulated experience of all those engaged in this kind of wórk bears strong testimony in favor of the prophylactic inoculations against hydrophobia as taught and practiced by Pasteur. At the bacteriological laboratory in Cuba 306 persons have been treated by the "double intensive" plan. Of these only 2 died after going through the full course,—a mortality of 1.63 per cent. All these cases were bitten by dogs proved experimentally and clinically to be rabid, or, at any rate, suspected. That the inoculations were conducted with due conservatism is indicated by the fact that only 306 persons were treated out of 700 applicants. Some of the failures Pasteur attributes to the long intervals between the prophylactic inoculations, and in grave cases he now advises that successive inoculations should be made with cord-substance twelve, ten, and eight days old, during the first twenty-four hours; on the second day with material six, four, and two days old; on the eighth day with material one day old, to be followed by two similar series of inoculations. By following this energetic plan of prophylactic treatment he has been able to secure protection even in the most urgent cases; that is, in cases where the stage of incubation had nearly terminated.

Palliative Treatment.—The nature of the disease should, under no circumstances, be disclosed to the patient, as the people, high and low, educated and ignorant, are only too familiar with the terrible suffering caused by this affection and its absolute certainty of a fatal termination in a few days. In one of my cases the patient had been made acquainted with the character of the ailment, and begged piteously that his life might be terminated by the administration of chloroform, knowing well that the intense suffering would continue to the last moment. As light, draughts of air, and noise of every kind increase the suffering by exaggerating convulsive spasms, these aggravating causes should be eliminated from the patient's room, and only a limited number of persons should be admitted to render the necessary assistance and carry out the directions of the attending physician. As the saliva of hydrophobic patients contains the specific virus, those placed in charge of the patient should protect themselves against inoculation by preventing the contact of the saliva with abraded surfaces, or, still better, by covering any abrasions which may exist with a collodium dressing. Thirst is quenched by administering water per rectum. Medicines by the mouth should not be given, as every attempt at swallowing brings on violent spasms of the muscles of deglutition and the respiratory muscles of the larynx. Morphia combined with small doses of atropia should be given subcutaneously in such doses and at such intervals as will procure rest. The subcutaneous administration of quinine and woorara has been advised, but both of these remedies are more harmful than useful, and neither of them either add anything to the duration of life or alleviation of suffering. The only remedy which can be relied upon to afford prompt relief is chloroform by inhalation. Ether should never be used, as the hyperæmic condition of the brain and spinal cord which is present in every case of hydrophobia sufficiently contra-indicates its use. The inhalation of chloroform must be conducted by an assistant or a competent, reliable nurse, and should never be carried beyond the point where relief is afforded, and it should be repeated as often as the paroxysms return.

CHAPTER XVII.

SURGICAL TUBERCULOSIS.

TUBERCULAR LESIONS furnish a most excellent illustration, clinically and under the microscope, of the origin, course, termination, and tissue changes of what is known as chronic inflammation. A histological description of a tubercular nodule is a description of the pathology of chronic inflammation. Tuberculosis in all its forms is caused by a specific microbe, the action of which upon the tissues produces histological and vascular changes which are characteristic of chronic inflammation. Of all the microbic diseases, with the exception of suppuration, tuberculosis is of the greatest interest and importance to the surgeon. Of the greatest interest because the tubercular lesions which come under his care are more clearly understood from a bacteriological stand-point than most of the other surgical diseases, and of the greatest importance on account of their great frequency. That large class of ill-defined lesions which were grouped under that indefinite and vague term *scrofula*, in the text-books of but a few years ago, have been shown by recent research to be identical with the recognized forms of tuberculosis, etiologically, clinically, and anatomically. In this chapter I shall aim to give a brief description, from a bacteriological and clinical stand-point, of such localized tubercular lesions which, by general consent, are regarded as surgical affections and requiring surgical procedures in their successful treatment.

HISTORY OF THE MICROBIC ORIGIN OF TUBERCULOSIS.

The first inoculation experiments with tubercular products were made by Kortum in 1789, and Cruveilhier in 1826. In 1834 Erdt succeeded in producing numerous nodules in the lungs of horses by inoculating them with tubercular pus, and Klencke, in 1843, produced tuberculosis in rabbits by intra-venous injections of tubercular matter. The results obtained from the crude inoculation experiments which were made years ago by Villemin pointed strongly toward the infectiousness of tuberculosis. Villemin's experiments consisted in the subcutaneous insertion, behind the ear of rabbits, of fragments of tubercular tissue or fluid taken from the cavity of a tubercular lung, recently removed from a patient who had died of pulmonary phthisis.

The first animal thus infected was killed three and a half months after inoculation. The lungs and most of the internal organs were found diffusely infiltrated with miliary tubercle. His numerous later experiments yielded similar results, and led him to the following conclusions: "Phthisis of the lungs (like tubercular diseases in general) is a specific infection. Its etiology depends on an inoculable agent. It can be readily communicated from man to animal by inoculation."

Vogel repeated the experiments of Villemin on horses without success. Biffi, Verga, and Sangalli experimented on mules, cows, sheep, dogs, cats, mice, and chickens with negative results. The experiments of Langhans led him to the conclusion that tubercle could not be communicated in the manner described by Villemin. He claimed that the inoculation material acted only the part of a foreign body, the inflammation following its insertion into the tissues differing in no way from the ordinary forms of inflammation. Among those who made successful inoculation experiments, and adopted the doctrines advanced by Villemin, may be mentioned Hèvard and Cornil, Hoffmann, Cohn, Béhier, Empis, Mantagazza, Bizzozero, Lebert and Wyss, Klebs, Koester, Waldenburg, Bijuen, Simon, Sanderson, W. Fox, Papillon, Nicol, and Laveran. Hèvard and Cornil were able to propagate them. They inoculated with genuine tubercular material, but failed with cheesy products. Marcet inoculated 11 guinea-pigs with the sputa of phthisical patients, and in 10 of them the experiment proved successful. Cohnheim injected tubercular material into the anterior chamber of the eye in rabbits, and succeeded in producing the disease artificially in this manner. Hueter produced tuberculosis of the iris by inserting into the anterior chamber of the eye in rabbits fragments of tubercular tissue. Toussaint showed that true tubercle, both in man and animals, reproduces itself indefinitely with absolutely constant and identical properties, and that it is quite capable of being transmitted from animal to animal without losing its virulence.

Krishaber and Dieulefoy experimented on monkeys, and the results obtained led to the conclusions: 1. That human tubercle, when inoculated, kills a monkey in nine out of ten cases, with lesions analogous to those met in man. 2. The effect of the inoculation varies according to the substance employed; the gray granulation is most, and the pulmonary parenchyma least, infectious. Schüller and Lentz made successful inoculations with blood taken from tuberculous rabbits. Lippl, Schwenniger, Tappeiner, and Weichselbaum succeeded in producing the disease in animals by inhalation. Successful feeding experiments were made by Chaveau, Aufrecht, and Bollinger. Since Villemin announced the inoculability of tuberculosis, diligent search was made to discover and isolate a specific micro-organism which should be characteristic of this disease.

The first cultivation experiments were made by Klebs in 1877. He found, by examining fresh specimens of tubercle of human beings, that they invariably contained bacteria. He cultivated them in egg-albumen and Bergmann's culture fluid, and found, by experiment, that the cultures produced the same effect in causing disease by inoculation as the tissues from which they were grown. Injections of the culture under the skin, into the muscles, lungs, pleural and peritoneal cavities, caused death of the animals from tuberculosis. Cultures made in a similar manner from scrofulous glands and lupus-tissue produced the same effect in animals. **Max** Schüller repeated the experiments of Klebs with the same results. He described the specific microbe as round and rod-shaped bacteria, the rods bulbous at both ends, composed of two, seldom more, spherical bodies. He found these microbes in great abundance in tubercular joints and tubercular foci in bone. He produced the disease artificially in animals which were previously inoculated by making contusions of joints. Other workers in the same field advanced theories, found and described microbes, which were supposed to bear a direct etiological relationship to tuberculosis, but nothing definite was known on the subject until the father of modern bacteriology, Robert Koch, in 1882, announced to the profession his great discovery. He had found and demonstrated the true and essential cause of tuberculosis, the bacillus of tuberculosis, and, in his first publication, brought such convincing proof of the correctness of his claim that, with few exceptions, it brought conviction even to the minds of the most skeptical. He had not only found the bacillus, but showed that it was present in all tubercular lesions. He had isolated and cultivated the bacillus from tubercular tissue; and, finally, he had furnished the crucial test—had produced tuberculosis, artificially, in animals by inoculation with pure cultures.

A number of pathologists who inoculated animals with non-tubercular material claimed that they had produced pathological conditions analogous to those found in animals which had been infected with the virus of tuberculosis. Fragments of sponge implanted in the abdominal cavity produce a condition which resembles tubercular inflammation, and it has been asserted that powdered glass has a similar property. Schottelins, Wargunin, Weichselbaum, and Martin have employed various substances by way of experiment, such as powdered cheese, brain-substance, lycopodium-seed, Cayenne pepper, and pulverized cantharides. They caused these to be inhaled in the form of a fine spray, with the result that they were almost invariably able to produce, in different animals, an eruption of nodules in the lung and sometimes in other organs.

With Limburger cheese Weichselbaum produced an eruption in the lungs and kidneys of dogs, after fifteen inhalations during seventeen days, which, histologically, could not be distinguished from the products of genuine tuberculosis. Further experimentation soon showed that these were instances of pseudo-tuberculosis; that, while the gross appearances of the lesions resembled true tuberculosis, inoculations with this material never reproduced the disease, while inoculations with tubercular tissue could be done through a series of animals without impairing the potency of the virus or varying the constancy of the results. Koch's discovery did not lead to such energetic search for the bacillus of tuberculosis among surgeons as physicians, because, as König asserts, the symptoms and signs of the tuberculous affections coming under the observation of surgeons are so characteristic that, for practical purposes, a correct diagnosis could be made in the majority of cases without a knowledge of their microbic nature and the improved methods for making a positive diagnosis derived therefrom. Koch himself, in the publication above referred to, demonstrated the presence of the bacillus in lupus, the so-called scrofulous glands, tubercular joints, etc. He called attention to the fact that in these affections the bacillus can be constantly found in giant cells and between the epithelioid cells, while it is more difficult to find it in cheesy products, unless caseation has taken place quite rapidly.

Koch examined 19 cases of miliary tuberculosis, in which bacilli were found in every nodule; 29 cases of phthisis, in every one of which bacilli were found most numerous, with the exception of the sputum, in recent caseous foci and in the walls of cavities undergoing speedy destruction. He also found them constantly in tuberculous ulcers of the tongue, tuberculous pyelo-nephritis, and tuberculosis of the uterus and testicles; also in 21 cases of tuberculosis of lymphatic glands. Further, in 13 cases of tuberculosis of joints and in 10 cases of tuberculosis of bone; in 4 cases of lupus, in which only a single bacillus could be seen in the giant cells; in 17 cases of Perlsucht in cattle. Finally, in animals inoculated with tubercular virus: 273 guinea-pigs, 105 rabbits, 44 field-mice, 28 white mice, 19 rats, 13 cats, besides dogs, chickens, pigeons, etc. Examinations of sputa and organs in various other non-tubercular affections for bacilli resulted, without exception, negatively.

Weichselbaum, Meisels, and Lustig found tubercle bacilli in the blood in cases of acute miliary tuberculosis, both during life and after death. Schuchardt and Krause examined 40 cases of tuberculosis of bones, joints, tendon-sheaths, and the skin in Volkmann's clinic, and never failed in finding bacilli, although in some specimens careful and prolonged search had to be made.

Schlegtendal examined 520 specimens of pus from tuberculous suppurations, and found bacilli present in about 75 per cent. of the cases. Mögling found the bacillus never absent in tuberculous pus from 53 patients. The literature on the etiological relation existing between the bacillus of tuberculosis and the affections of the skin, glands, bones, and joints, which have heretofore been grouped under the head of scrofula, is immense; but the foregoing quotations will suffice to show the regularity with which the bacillus can be found in the tissues of the so-called scrofulous affections, as well as in all recognized clinical forms of tuberculosis.

DESCRIPTION OF BACILLUS TUBERCULOSIS.

The tubercle bacillus, with the exception of the bacillus of septicæmia in mice, is the smallest of the known bacilli. The length of each rod varies from one-fourth to three-fourths of the diameter of a red blood-corpuscle. The thickness corresponds to that of the bacillus of sepsis in mice. The rods are either straight or, what is more common, bent or curved near the centre.

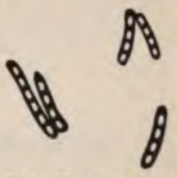

FIG. 92.—TUBERCLE BACILLI CONTAINING SPORES. Zeiss, $\frac{1}{18}$ 0.4. (*Koch.*)

In cultures and in the tissues they occur singly, in pairs, or in bundles. In a state of fructification the bacilli contain from two to six spores. In stained rods the spores appear as clear, minute, ovate spaces, as they are not affected by the coloring material. In some bacilli the spores form slight projections on the sides of the rod. Reproduction by spore formation also takes place in the tissues within the animal body. In badly-stained specimens, and on superficial examination, the spores impart to the bacillus the appearance of a chain coccus; but, examined closely, it is seen that the protoplasm of the bacillus is continuous, and the apparent interruptions are due to the presence of the spores. The bacilli of tuberculosis are non-motile, and consequently possess no power of locomotion, and cannot penetrate into the tissues without assistance. In the tissues they are found in the interior of giant cells and within and between epithelioid cells. They are constantly found in places where the tuberculous process is commencing or actively progressing. In the beginning they are isolated and in the interior of cells; later, they become more abundant and form groups. In cheesy deposits they are either entirely absent or few in number. The virulence of caseous material is due mostly to the presence of spores, which may remain in a latent condition and yet retain their power of reproduction under more favorable conditions for an indefinite period of time. As soon as giant cells appear, they contain bacilli in their interior, as a rule. In some giant cells only one bacillus can be found, and then it occupies a part of the cell which contains no nuclei.

In giant cells with numerous bacilli the latter arrange themselves around the periphery in the interior of the cell, while the centre contains few or none.

The first ingress of bacilli into the diseased tissues probably takes place by wandering cells, which transport the non-motile microbe. In many inoculation experiments such bacilli-containing cells have been found in the blood and tissues.

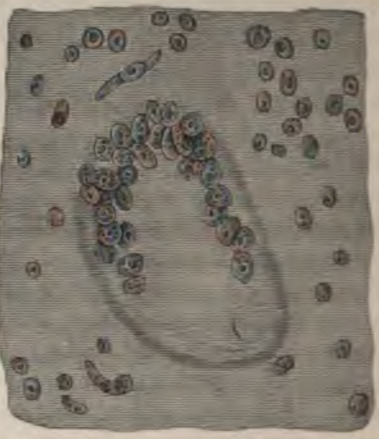

FIG. 93.—GIANT CELL WITH ONE TUBERCLE BACILLUS. SECTION FROM LUPUS OF SKIN. 700:1. (*Fluegge.*)

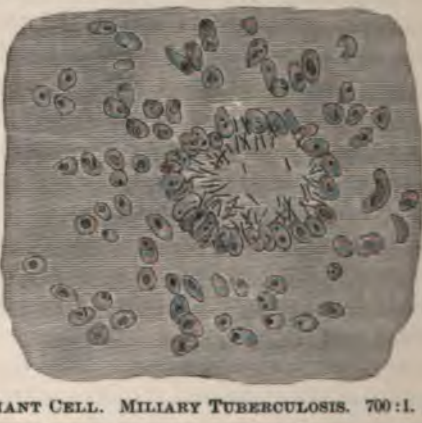

FIG. 94.—GIANT CELL. MILIARY TUBERCULOSIS. 700:1. (*Fluegge.*)

Staining.—The peculiar behavior of the bacillus of tuberculosis to different staining material enabled Koch not only to discover this microbe, but also to differentiate it from all other microbes. While the aniline dyes and other nuclear staining material showed no micro-organisms in tubercular products, the bacillus came plainly into view if a small quantity of alkali was added to the aniline solution. Later experience proved that the same effect is produced if, instead of an alkali, anilin, tolnidin, turpentine, carbolic acid, or ammonia is added. All of these substances aid the penetration of the staining fluid into the bacillus. Of especial advantage is the discovery, also made by Koch, that the staining fluid is fixed more permanently by treating the sections stained with alkaline aniline dyes with nitric or muriatic acid, a procedure which removed the staining from the cells, nuclei, and all other bacteria, while the tubercle bacillus alone remains stained. The preparation is further completed by staining once with one of the ordinary aniline dyes, which stains the cells and nuclei and other bacteria, so that the tubercle bacillus, for instance, appears red, the nuclei and other bacteria blue.

Most of the bacilli in Fig. 95 contain spores, the majority of them slightly curved or bent; they lie free,—that is, outside the cells. Where they appear to be within the cells, a close examination shows them to be either upon or underneath the cells.

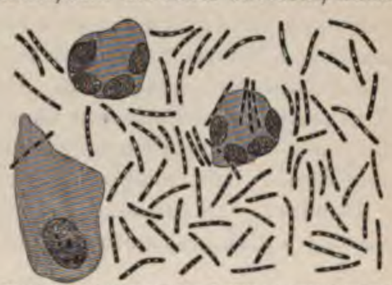

FIG. 95.—COVER-GLASS PREPARATION FROM PHTHISICAL SPUTUM. DOUBLE STAINING, AFTER EHRLICH'S METHOD, × 1500. (*Baumgarten*.)

For section-staining Ehrlich's method is the best:—

Saturated alcoholic solution of methyl-violet or fuchsin, . .	11 parts.
Aniline water, ...	100 "
Absolute alcohol, ...	10 "

Sections are left for twelve hours in this solution. Treat the specimens with 1-to-3 solution of nitric acid a few seconds; wash in alcohol (60 per cent.) for a few minutes; after-stain with diluted solution of vesuvin or methylene-blue for a few minutes; wash again in 60-per-cent. alcohol; dehydrate in absolute alcohol; clear with cedar-oil; mount in Canada balsam.

The examination of fluids for bacilli can be done rapidly and most satisfactorily by Gibbes' method:—

GIBBES' MAGENTA SOLUTION.

Magenta, ...	2 parts.
Aniline oil, ...	3 "
Alcohol (specific gravity 0.830), ...	20 "
Distilled water, ...	20 "

Stain cover-glass preparations in this solution for fifteen or twenty minutes; wash in 1-to-3 solution of nitric acid until the color is removed;

rinse in distilled water; after-stain with methylene-blue, methyl-green, iodine-green, or a watery solution of crysoidin, five minutes; wash in distilled water until no more color comes away; transfer to absolute alcohol for five minutes; dry, and preserve in Canada balsam.

Cultivation.—The best culture medium for the bacillus of tuberculosis is solid, sterilized blood-serum of the cow or sheep, with or without the addition of gelatin, at a temperature of 37° to 38° C. (98.6° to 100.4° F.). The bacillus grows very slowly, and only between the temperatures of 30° and 41° C. (86° and 105.8° F.). In about a week or ten days the culture appears as little, whitish or yellowish scales and grains. Cultivations can also be made in a glass capsule or solid blood-serum, and the appearance of the growth studied under the microscope. The scales or pellicles are then seen to be made up of colonies of a perfectly characteristic appearance. The growth ceases after three or four weeks. The blood-serum is not liquefied unless putrefactive bacteria contaminate the culture. Fränkel figures, in his "*Atlas der Bacterienkunde*," a luxuriant culture of the bacillus of tuberculosis upon glycerin-agar.

Nocard and Roux have found that coagulated blood-serum is improved for the growth of the bacillus by adding peptone, soda, and sugar. A further addition of 6 to 8 per cent. of glycerin favors the growth of the bacillus still more, while, at the same time, it prevents the formation of a dry crust upon the culture medium, which otherwise forms by evaporation. They also made successful cultivations upon agar-agar bouillon, to which was added 6 to 8 per cent. of glycerin, kept at a temperature of 39° C. (102.2° F.).

Koch has cultures 3 years old which have passed through 40 generations and still retain their virulence, showing plainly the longevity and tenacity of the bacillus of tuberculosis.

INOCULATION EXPERIMENTS.

Long before the discovery of the bacillus of tuberculosis by Koch, genuine tuberculosis was produced artificially in animals by inoculation with the products of tubercular inflammation. Hueter inoculated the anterior chamber of the eye in rabbits with lupus-tissue, and produced typical tuberculosis of the iris. Schüller introduced fragments of lupus-tissue directly into the veins of animals, and in this way caused pulmonary tuberculosis. Koch produced tuberculosis in animals susceptible to this disease by implantation of tubercular tissue in various localities and by inoculation with pure cultures, the experiments yielding, almost without exception, positive results. The same author inoculated the anterior chamber of the eyes in 18 rabbits from 5 cases of lupus, and in all of them tuberculosis of the iris was produced, and, if life was prolonged for a sufficient length of time, was followed by tuberculosis of the lymphatic glands of the neck, lungs, kidneys, liver, and spleen. Similar results were also obtained in 5 guinea-pigs. Cornet has made numerous experiments, in Koch's laboratory, on animals, to ascertain the inoculability of tuberculosis through abrasions of the skin, or a pure culture of tubercle bacilli is applied to a cutaneous abrasion; the result in most, if not all, cases is a local tuberculosis in the adjacent lymphatic glands, and, later, a general miliary tuberculosis.

The same author made, more recently, a long series of experiments on dogs, to ascertain the different avenues through which tubercular infection is known to take place. Tubercular sputum and pure cultures inserted into the lower conjunctival sac in healthy dogs produced tissue hyperplasia at the seat of inoculation, and was followed by infection of the cervical glands on the corresponding side. Some of the glands underwent caseation, and the presence of bacilli could be demonstrated in all of the pathological products. In other animals the tubercular material was introduced into the nasal cavity. The cervical glands, especially those on the corresponding side, became enlarged and caseated. Infection through the mouth, by depositing the tubercular material in a depression made with a blunt instrument between the canine teeth, resulted also in tuberculosis of the glands of the neck. Infection of the external meatus of the ear, without creating an infection-atrium intentionally, was followed by infection of the lymphatic glands behind the ear and along the neck on the same side. Cutaneous tuberculosis in the form of an ulcerating lupus was produced by shaving the skin on one side of the nose and face, and scratching it with a finger-nail infected with a pure culture. Injection of pure cultures into the healthy vagina of bitches resulted in local tuberculosis and secondary infection of the inguinal glands. Inoculations of other parts were followed by the same train of symptoms,—local tuberculosis at the seat of infection, followed by dissemination of the process along the course of lymphatic channels. The lungs were found affected only in two of the animals. These experiments show conclusively that the bacillus of tuberculosis, introduced through superficial peripheral infection-atria, seeks the lymphatic channels, through which it is extensively disseminated before general infection takes place. Cornil and Leloir implanted lupus-tissue into the peritoneal cavity of guinea-pigs, and in 5 cases out of 14 experiments produced peritoneal and general tuberculosis. Pagenstecher and Pfeiffer took the secretion of the conjunctiva from patients suffering from lupus of this structure, and injected it into the anterior chamber of the eye in rabbits. After five to six weeks nodules could be seen on the surface of the iris, which, on examination, were found to be in every respect identical with tuberculosis of this organ. Doutrelepont inoculated the peritoneal cavity in 50 guinea-pigs, and in 8 rabbits the anterior chamber of the eye with the same material, with the result that in all of the animals local tuberculosis was produced at the point of inoculation, and in 3 of the guinea-pigs and in 1 rabbit the local disease was followed by general tuberculosis.

Inoculations with material from so-called scrofulous glands produce the same effect as when lupus-tissue is used, and we are, therefore, forced to conclude that these glands owe their existence to the same cause. Arloing prepared an emulsion from a scrofulous (tubercular) gland, caseous in its centre, which was taken from a boy aged 14. This was injected beneath the skin of 10 rabbits, and the same number of guinea-pigs. Visceral tuberculosis developed in all of the guinea-pigs, but the rabbits remained healthy, except that 2 showed yellow, caseous granulations at the seat of inoculation. Some glands excised from the neck of a young woman produced tuberculosis both in rabbits and guinea-pigs. The patient died three weeks after the operation from miliary tuberculosis. From these experiments he inferred that either scrofula and tuberculosis were nearly allied affections, but caused by different agents, or they were derived from the same virus, of which the activity was modified in the scrofulous form.

That the number of bacilli injected has a great deal to do with the result has recently been satisfactorily demonstrated by Bollinger. He found that infectious milk from a tuberculous cow, which produced local tuberculosis by intra-peritoneal injections, lost its virulence if diluted from 1:40 to 1:100. The sputum of phthisical patients was found much more virulent, and had not lost its power to produce tuberculosis on being diluted 1:100,000, on being injected into the abdominal cavity, or the subcutaneous connective tissue. Feeding experiments with sputum diluted 1:8 yielded negative results. Pure cultures remained virulent when diluted 1:400,000. All the experiments proved that the more concentrated the material and the greater the number of bacilli, the more rapid and intense was the development of the lesion caused by the injection. It was estimated that about 820 bacilli were necessary to produce tuberculosis in guinea-pigs. Intra-peritoneal injections did not always produce peritoneal tuberculosis, and in cases where this did not occur the organs affected were the lymphatic glands, spleen, lungs, liver, kidneys, and genital organs, in the order of frequency named, showing conclusively that localization does not invariably take place at the point of primary infection.

Direct intra-venous infection by injections of pure cultures, suspended in distilled water, is the most effective way in which diffuse miliary tuberculosis can be artificially produced in animals with unfailing certainty. Koch succeeded also in producing the disease in rabbits, guinea-pigs, rats, and white mice, by inhalation. A pure culture, suspended in distilled water, was used with a hand-spray, and the cages in which the animals were kept were filled with the infected spray. The animals were killed after twenty-eight days, and all of them showed unmistakable signs of pulmonary tuberculosis.

INOCULATION-TUBERCULOSIS IN MAN.

The opinion that tubercle is capable of inoculation was held by ancient writers, and Lænnec, himself, after a nick from a saw while making a necropsy on a phthisical subject, thought that he witnessed an example of inoculation in a small tubercle in the skin, but twenty years afterward this distinguished clinician was in good health, though finally he died of phthisis.

Schmidt made a number of experiments to ascertain the effect of inoculations of superficial abrasions of the skin with the virus of tuberculosis. In guinea-pigs he made abrasions in the skin, to which he applied tubercular material and covered the point of inoculation with collodium. All of his experiments failed in producing tuberculosis, while in the control animals, in which the infectious material was introduced into the subcutaneous tissue, or into the peritoneal cavity, tuberculosis developed without a single exception. He believes that the results of these experiments are only corroborative of the assertion previously made by Bollinger and Koch, that the susceptibility of the cutis for tubercular infection is slight. A sufficient number of authenticated cases, however, have been reported during the last few years, to prove that in man tuberculosis is not infrequently contracted by the absorption of tubercular material through small wounds and superficial abrasions of the skin. Volkmann, a number of years ago, made the statement that tubercular infection never takes place through a large operation wound, or at the site of severe injuries, but that localization of the bacillus is likely to take place in parts the seat of very slight contusions, or what may appear at the time as an insignificant injury. He explained this by assuming that the active tissue changes which take place during the process of regeneration after a severe trauma prevent the infection.

In studying the cases of inoculation-tuberculosis, which will be referred to below, it will be seen that the infection-atrium was always caused by a trivial injury. A very interesting case of inoculation-tuberculosis came under my own observation during the last year. The patient was a strong, healthy young woman, with a good family history, who was employed in a rag establishment in sorting rags. Two months before she came under my care she noticed a small sore on the dorsal side of the right index finger, near the metacarpo-phalangeal joint. The place ulcerated, and the granulation tissue which appeared melted rapidly away, forming a deep excavation, which had the extensor tendon for its floor. Two weeks later a nodule appeared in the course of the lymphatic vessels, near the elbow-joint, over the anterior aspect of the arm, which was soon followed by the formation of three other nodules between this point and the primary seat of infection. General health not impaired in the least. Inflamed foci neither painful nor tender on pressure; presented distinct evidences of fluctuation. All the foci were excised and presented the characteristic appearances of tubercular tissue. The primary focus, after excision, left such a large defect that it was found impossible to close the wound by suturing, and consequently the surface was covered with Thiersch's grafts taken from the arm. Primary union of all the sutured wounds and speedy, definitive healing of the defect at the primary seat of infection.

There can be no doubt whatever that in this case infection occurred through a small wound of the index finger, by handling contaminated rags, which was followed by dissemination of the bacilli through the lymphatic vessels in direct communication with the primary infection-atrium. I have had also under treatment a well-marked case of extensive subcutaneous tuberculosis of the hand, in the person of the mother of several children who had died of pulmonary tuberculosis. The disease originated near the tip of the index finger, at the site of a former abrasion, in which a papillomatous swelling formed. This ulcerated and healed partly, when the disease commenced to spread along the subcutaneous connective tissue, and when the patient came under my observation it had extended almost over the entire dorsum of the hand. A number of fistulous openings existed, which discharged daily only a few drops of thin, serous pus. The subcutaneous tissue was transformed into a mass of granulation tissue, which was removed with a small spoon through multiple incisions, and the wound surfaces were freely iodoformized. The process of repair was slow, but satisfactory. Martin du Magny has collected the clinical material of cases of inoculation-tuberculosis, and in his comments upon the cases asserts that the sputum of phthisical patients and animal excretions were the usual carriers of the bacilli; consequently the affection is most frequently met with among physicians, nurses, butchers, and teamsters. The external appearances, manifested at the point of inoculation, consist in the formation of a red nodule in the skin, which increases slowly in size and forms miliary abscesses, in which papillomatous proliferation takes place, and around which a new zone of infiltration forms, which in turn again suppurates and becomes papillomatous. The centre heals with the formation of a flat cicatrix, while the destructive process progresses slowly in a peripheral direction.

Hanot has collected 6 cases, 1 of which came under his own observation. In this case the patient was in the third stage of phthisis, and died soon after from a tubercular ulcer on the arm of at least two years' standing, while the history of cough only dated from the last two months, which would show that the cutaneous lesion preceded the pulmonary, and was the cause of the phthisis. In the cases which he collected the sources of inoculation were necropsies on tubercular patients, handling old bones, pricking the hand with a fragment of porcelain from the broken spittoon used by a phthisical patient, and in 4 of the cases the tubercular character of the cutaneous lesion was verified by finding the bacilli.

Eiselsberg has observed 4 cases of inoculation-tuberculosis during the last few years. The first case was a girl 16 years old, in whom the disease developed in the track of a perforation of the lobe of the ear made preparatory to the wearing of an ear-ring, and which was kept from closing by the insertion of a thread. The tubercular product appeared in the shape of a hard swelling the size of a hazel-nut. The second case was a young man who injured himself with the point of a knife above the external epicondyle of the humerus. Eighteen days later a swelling, the size of a pea, appeared at the site of injury, with an ulcerated surface covered by pale, flabby granulations. In the axilla of the same side one of the lymphatic glands was found enlarged to the size of a hazel-nut. The third case concerned a woman 50 years of age, who was supposed to have infected herself by washing the clothes of a person the subject of a tubercular abscess of the spine, and who with her fingers scratched an acne pustule on her face. At this point, six to eight days later, a painful swelling, the size of a pea, formed, which subsequently became indurated, and opened spontaneously in six weeks. At the end of three months the place of inoculation presented an ulcer with indurated margins. In the fourth case the inoculation followed in the track made by the needle of a hypodermic syringe, in a girl 20 years of age. The swelling which appeared opened after six weeks, and a small quantity of pus was discharged. Four months subsequently the fistulous opening communicated with an abscess-cavity, the size of a silver dollar, lined by a wall of granulation tissue. In all of these cases no evidence of tuberculosis could be detected in any of the internal organs, and the local disease could be traced in every instance to some antecedent lesion, through which the infection had evidently taken place. The diagnosis in all cases was based on an examination of the granulation tissue for the bacillus of tuberculosis, which was always found present.

Another case of tubercular infection through ear-rings is related from Vienna in a girl, 14 years of age, of a perfectly healthy family, who wore ear-rings left to her by a friend who had died of pulmonary tuberculosis. Soon ulcers appeared on the lobes of both ears, the cervical glands became swollen, and percussion and auscultation revealed infiltration of the apex of the left lung. Tubercle bacilli were found in the ulcers and sputa. This case is only another instance of inoculation-tuberculosis, where, from the point of infection, the disease extended along the lymphatic system, and, finally, systemic infection from the entrance of bacilli into the general circulation.

In the cases of inoculation-tuberculosis cited above, infection occurred through some slight lesion, puncture, or abrasion, which furnished the necessary infection-atrium for the entrance of the bacillus into the tissues, but a number of cases have been reported by reliable observers where infection took place through a larger wound or granulation surface. Middeldorpf reports the case of a healthy carpenter, who opened his knee-joint by the cut of an ax, and dressed the wound with a soiled handkerchief. The wound healed kindly, but later the joint became swollen, tender, and painful. Resection was performed, and on examining the capsule it was found very much thickened. In the granulation tissue tubercle bacilli were found. Wahl amputated the arm of a boy suffering from gangrene, the result of an injury, and discharged the patient with the wound completely healed, except a small granulation surface from which the drainage-tube had been removed. At first the wound was dressed by a girl suffering from tuberculosis. The wound soon showed all the characteristic appearances of fungous disease, and the lymphatic glands became infected from this source. I have seen in numerous instances large wounds made for the removal of tubercular glands become infected a week or two after the operation, after the superficial wound had apparently healed. In such cases the overlying cicatrix is subsequently completely destroyed by the granulations underneath. The energetic use of the sharp spoon and free iodoformization are the only resources in finally effecting the healing of such wounds. König has seen 16 cases of inoculation-tuberculosis, following operations for tubercular disease of bones and joints, and 2 such cases have been described by Kraske. Czerny reports 2 cases in which tuberculosis followed in wounds treated by Reverdin's method of skin-grafting. In both instances the patients were healthy, and the skin-transplantation was made during the treatment of extensive burns. The skin was taken from limbs amputated for tubercular affections. In both cases tuberculosis of the adjacent joint occurred, and in 1 of them tuberculosis of the granulating surface. A number of cases of inoculation-tuberculosis following circumcision are on record, in which the infection often occurred in the practice of orthodox Jews, who performed the operation in accordance with the directions laid down in the Mosaic laws. The loose connective tissue of the prepuce, richly supplied with lymphatics, is an admirable surface for absorption, and, when infectious material is brought in contact with it, furnishes the most favorable conditions for the production of local lesions and the transportation of microbes along the lymphatic channels to more distant parts.

Lehmann has observed 10 cases of inoculation-tuberculosis in Jewish boys, caused by sucking the wound after ritual circumcision by a phthisical person. Ten days after the circumcision the wound became the seat of ulceration, and the inguinal glands began to enlarge. Four of the children died of tubercular meningitis, and 3 died after a prolonged illness caused by multiple tuberculár abscesses. Hofmokl has reported a similar case, and Weichselbaum detected the bacillus of tuberculosis in the circumcision wound.

Elsenberg has described 3 cases of tubercular infection after circumcision. All the cases were infants, and the disease appeared primarily in the wound or cicatrix, and, later, in the inguinal glands. Local treatment by scraping proved successful. The diagnosis was corroborated by microscopical examinations of the granulation tissue. Willy Meyer relates a case in which circumcision was performed according to the rules of the Jewish Church eight days after birth by an old man, and in which four weeks after the ceremony an induration appeared at the frenulum, and the inguinal glands about the same time began to enlarge. Syphilis was suspected, and the little patient was put on a specific course of treatment. The inguinal glands suppurated, and another small abscess formed in the right gluteal region. The diseased tissue about the glans penis was then excised. Microscopical examination of the granulations revealed the presence of miliary tubercles and bacilli in great abundance. The above cases furnish abundant and convincing proof of the possibility of the transmission of tuberculosis by cutaneous inoculation through superficial abrasions, small wounds, and granulating surfaces, and this subject is deserving of the most careful attention of surgeons in the matter of prophylaxis, diagnosis, and treatment.

HISTOLOGY OF TUBERCLE.

A tubercle-nodule is an aggregation of cells primarily invisible to the naked eye, the product of a minute focus of inflammation, caused by the presence of the essential cause of tuberculosis. When the nodule becomes so large that it can be recognized without the aid of the microscope, it already consists of a confluence of a number of minute microscopic nodules. Lænnec described four varieties of tubercle: 1. Miliary tubercle, where the visible product of tubercular inflammation appears as nodules the size of a millet-seed, of a grayish color, and usually arranged in groups. 2. Crude tubercle, where the miliary nodules have become confluent and have undergone caseous degeneration. 3. Granular tubercle, where the nodules are extremely small, nearly the size of a millet-seed, and scattered uniformly through a whole organ. They are not arranged in groups and have no tendency to become confluent. In the centre they become transformed into yellow tubercle. 4. Encysted tubercles, or such as are constituted of a hard mass of crude tubercle in the centre surrounded by a firm fibrous capsule. These varieties only represent different phases of the same process and different stages of inflammation produced by the same cause. The anatomico-pathological basis of tubercle was created by Virchow, and has been firmly established through the laborious researches of Langhans, Wagner, Klebs, Schüppel, Rindfleisch, Koester, Friedländer, Fox, Baumgarten, and many others. The specific-cell theory has had many able advocates, and has been the subject of many animated discussions, but it has at last been abandoned as fallacious and unscientific. There are no specific tubercle-cells.

Lebert's tubercle-corpuscle is a thing of the past, and is only referred to as a landmark in the history of tuberculosis. Reinhart showed that these cells, which were regarded by Lebert as characteristic and pathognomonic of tubercle, could be found in all products of chronic inflammation, and their presence was only an evidence that a certain amount of inflammation existed. When we speak of a tubercle, we mean a nodule or granule, which is composed of leucocytes derived from the capillary vessels damaged by the bacillus of tuberculosis, or new cells derived from tissue proliferation of pre-existing cells acted upon by the same cause. The anatomical character of the nodule consists not in the presence of any particular cell-element, but in the peculiar arrangement of the cells; and this feature is the only reliable anatomical guide in making a diagnosis by the use of the microscope. The product of tubercular inflammation occurs either in the form of submiliary, microscopic granules, visible miliary nodules, or a cheesy infiltration, which may occupy an entire organ, as a lymphatic gland, or large, isolated foci, as in bone. Every tubercular product commences as submiliary nodules, which, when they become confluent, are transformed into visible gray miliary nodules, which again coalesce after they have undergone caseous degeneration from cheesy masses, which may be either small and circumscribed or large and diffuse.

Virchow defines tubercle as a nodule representing a heterogeneous growth, a product originally necessarily of a cellular nature, taking its starting-point from the connective tissue or from other mesoblastic structure, as marrow, fat, or bone. He asserts that the microscopic or submiliary granule contains all of the essential histological elements of tubercle, and by aggregation forms the ordinary miliary nodule of Lænnec. When the nodules become confluent they may form masses the size of a walnut, surrounded by a common zone of embryonal tissue. The yellow tubercle, the crude tubercle of Lænnec, is a more advanced stage of the gray, the histological elements of the latter having undergone caseation.

HISTOGENESIS OF TUBERCLE.

Colberg asserts that tubercles in the lungs originate from the nuclei of the capillary vessels and the connective tissue, the epithelial cells lining the alveoli never being primarily affected. Bastian observed tubercle-nodules upon the small vessels in cases of basilar meningitis, but refers their origin not to proliferation of the nuclei of the endothelial lining of the vessels, but to new cells springing from the endothelial cells of the perivascular lymphatic sheaths which surround the vessels of the meninges of the brain.

Knauff demonstrated the lymphoid character of the adventitia by examining the capillary vessels of the visceral pleura in dogs which had been exposed for a long time to an atmosphere impregnated with coal-dust. He found the pigment lodged in small masses close to the walls of small arteries and veins. Examining the same vessels in other dogs not thus treated, he found upon the outer surface of the adventitia opaque, whitish-gray nodules, surrounded by round and oval cells containing nuclei, also lymph-corpuscles. The same structures, which he named lymph-nodules, are also found around the same vessels of the pleura in man, and Knauff looks upon these lymphoid structures as the starting-point of tubercular inflammation.

Klebs maintains that the endothelial cells of lymphatic vessels are the most frequent location for the formation of the primary tubercle-nodule. He observed that in cases of tubercular ulceration of the intestines the peritoneum is reached through the lymphatic vessels. Silver-stained preparations of inoculation-tuberculosis in rabbits showed that the most recent products occurred in the interior of the lymphatic vessels at points of intersection. In some places the nodules extended into the tissues between the lymphatic vessels, but their centre always corresponded to the location of a lymphatic vessel. At some points the nodules were seen to branch out, but these projections, in reality, were within the lymphatic vessels, as the net-work of lymphatic endothelia could be seen above and underneath the tubercular product. Toward the centre of the nodule no endothelial cells could be distinguished, and this fact led him to the belief that the endothelial cells are directly concerned in the production of the new tissue. In the mesentery he saw the tubercles adhere to the outer wall of the capillary vessels, and, as the spindle-shaped cells of the outer coat appeared to be pushed apart by the new tissue, he regards the adventitia as a genuine lymphoid structure. Rindfleisch traces the beginning of the process in miliary tuberculosis of the lungs to a proliferation of the endothelia and the external connective-tissue layer of the capillary lymphatic vessels. Edward Smith believes in the epithelial origin of tubercle. Manz studied the development of tubercle in the choroid in patients suffering from general miliary tuberculosis. So constantly does this disease show itself in this structure that von Graefe, Cohnheim, Fränkel, and Bouchut recommend ophthalmoscopic examination as a diagnostic measure in cases of suspected pulmonary or general tuberculosis. Manz traces the commencement of the disease in the choroid to cell-pullulation in the tunica adventitia of the small vessels. The process is, however, not limited to this structure; the non-pigmented stroma-cells may also assist in furnishing material for the new product. Bart, on the other hand, asserts that the vessels, in cases of tuberculosis of the choroid, are not primarily affected; according to his observations, the process depends exclusively on a degeneration of the stroma-cells, as the remaining tissue did not appear affected.

Cohnheim, Ziegler, and others maintain that the leucocytes furnish most of the material in the building up of the tubercle-nodule.

Experiments on animals, as well as microscopic examinations of pathological specimens, have sufficiently demonstrated the fact that the tubercle-nodule is nothing more nor less than a circumscribed inflammatory product, the histological elements of which are composed of new tissue, formed by proliferation of fixed tissue-cells which have come in contact with the bacillus of tuberculosis or its ptomaines. The specific pathogenic effect of the bacillus consists in its power to cause a chronic inflammation of the tissues in which it has localized or with which it has been brought in contact. The tissues affected are the cells which are nearest the essential microbic cause, irrespective of their embryological origin, their histological structure, or physiological function. In cases of inoculation-tuberculosis the primary nodule develops at the point of insertion of the virus from connective-tissue proliferation, and from here the bacilli enter the lymphatic channels, and the secondary nodules are composed of cells derived from the endothelial, lymphoid, and connective-tissue cells which compose these structures. If the bacilli are injected directly into the circulation or gain entrance into the blood-current from some tubercular focus, they become implanted upon the wall of distant capillary vessels, and the nodule which forms at the seat of implantation consists of cellular elements formed by the tissues of the vessel-wall. As soon, however, as bacilli reach the extra-vascular tissues, they, in turn, furnish their part of the material for the further growth of the nodule. If the tubercle bacillus becomes implanted upon a mucous surface, as the bladder, intestines, nose, larynx, uterus, etc., if such surface is susceptible to tubercular infection, the epithelial cells take an early and active part in the inflammatory process. From the manner of entrance into and diffusion through the tissues, it is apparent that the mesoblastic tissues, the connective-tissue and endothelial cells, being the first to become infected, furnish the greatest amount of material in most tubercular lesions; but all tissues, when infected, take part in the process.

HISTOLOGICAL STRUCTURE OF TUBERCLE.

The essential histological elements which make up a primary tubercle-nodule are: (*a*) leucocytes; (*b*) giant cells; (*c*) epithelioid cells; (*d*) reticulum.

Leucocytes.—One of the convincing proofs of the inflammatory nature of tuberculosis is the presence of leucocytes in the tubercle-nodule. The bacillus of tuberculosis appears to exercise only a mild pathogenic effect on the capillary wall, and the primary inflammatory product is always scanty. As the colorless blood-corpuscles can only escape, in considerable number, through inflamed capillary walls which have undergone alteration from the action of some specific microbic cause, it is evident that its migration into the para-vascular tissues, where it forms a part of the tubercular product, can only occur after such alteration has taken place from the action of the bacillus upon the cement-substance of the endothelial lining of the capillary vessels. The leucocytes are found scattered among the other cellular elements, and are found in greatest abundance toward the periphery of the nodule. The leucocytes invariably undergo degenerative changes, and are never transformed into other forms of cells found in the tubercular product. They have been described as lymphoid corpuscles. Although constantly present, they are most numerous when the process is acute.

Giant Cells.—A great deal has been said and written concerning the origin and diagnostic value of the giant cells in the tubercle-nodule. They resemble the giant cells found in some forms of sarcoma, and appear to be simply certain cells which have outgrown others by taking up a greater amount of nourishment in the shape of leucocytes which have undergone fragmentation.

The giant cells, or, as Klebs calls them, *macrocytes*, are finely granular, and contain multiple nuclei, which usually occupy the periphery of the cell, or are arranged in a crescent at one end. In tubercular lesions artificially produced in animals the giant cells contain numerous bacilli, which occupy, as a rule, the peripheral zone of the cells. In tuberculosis in man the bacilli in these cells are never so numerous, and as central degeneration of the cells appears they disappear in this portion of the cell, while some may still be found in the periphery. During the progress of the disease the giant cell becomes more and more fibrous toward the periphery, at the expense of the protoplasmic part in the centre. The protoplasm evidently is transformed into or secretes the fibrous margin. If caseation does not take place the bacilli disappear, and the whole cell mass, including the giant cells, is converted into a cicatricial mass.

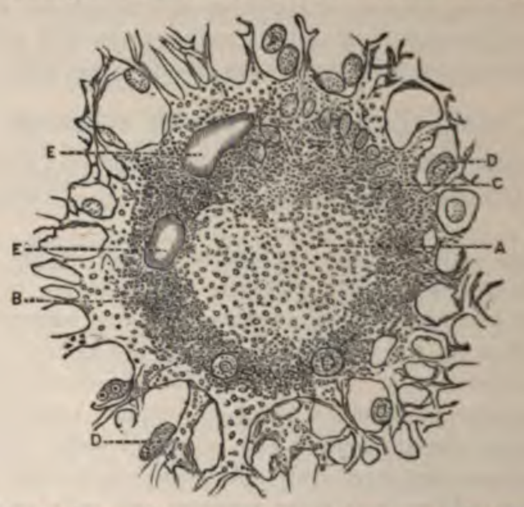

FIG. 96.—GIANT CELL FROM CENTRE OF TUBERCLE OF LUNG. × 450. (*Hamilton.*)
A, granular protoplasmic centre; B, peripheral more-formed part; C, crescent of nuclei; D, endothelium-like cells; E, two vacuoles within the giant cell.

The first evidences of degeneration appear in the centre of the giant cells, and, according to Weigert, they consist of structural and chemical changes which are indicative of coagulation necrosis.

In a recent tubercle-nodule the giant cells occupy the central portion, around which the epithelioid cells and leucocytes are arranged. The vacuoles are necrotic foci within the cells.

The giant cell found in tubercular tissue has its prototype in normal tissue. Giant cells were first discovered in normal tissue (marrow of bone) by Robin, who called them *myeloplaques*. They were subsequently accurately described by Virchow. In a normal condition they are constantly found in bone and the placenta. They are also found occasionally in fat-tissue, especially in cases of rapid emaciation. Kundrat has found them in inflamed serous membranes, and Stricker and Heitzmann in the inflamed cornea. They are always found around foreign bodies, becoming encysted in the tissues. Friedländer found them present in the aveoli of the lungs in cases of chronic pneumonia.

Heubner found giant cells in endarteritis, Baumgarten in gummata, Buhl and Jacobson in granulating wounds, and finally Jöhne and Pflug in actinomycotic foci. The histological source of these cells in tubercular affections has been traced to epithelial cells by Zielonko and Weigert; to endothelial cells by Kundrat, Klebs, Herrenkohl, and Zielonko; to connective tissue or endothelial cells by Virchow, Fleming, and Ziegler. Schueppel and Rindfleisch believe that they invariably originate within blood-vessels or lymphatics, where these authors regard them as the first step toward the development of tubercle-nodules. Ziegler claims to have seen giant cells develop from white blood-corpuscles. Hering, Aufrecht, Woodward, Schueller, and Treves are of the opinion that what appears as giant cells in tubercular tissue are not cells, but only represent spaces which correspond to transverse sections of lymphatic channels, the protoplasm representing the coagulated lymph within these vessels, and what appear as nuclei being enlarged, swollen endothelial cells. Giant cells possess amœboid movements, and by virtue of these they are capable of taking up in their protoplasm fine particles, such as microbes, pigment material, and blood-corpuscles, which have undergone fragmentation. The giant cells in tubercular lesions are hyperplastic, epithelial cells, and consequently are derived from the same histological source as these.

Epithelioid Cells.—Cells intermediate in size between the giant cells and the leucocytes are found in every tubercle-nodule in which the cells have not been destroyed by caseation. These cells were first described by Rindfleisch, and were called by him *epithelioid cells* from their structural resemblance to epithelial cells. Klebs calls them *platycytes.*

They are about two or three times larger than a white blood-corpuscle, and in shape they are either round or somewhat elongated. In structure they are finely granular, and contain one large and often a number of small nuclei. They form the bulk of all recent nodules, are scattered between the giant cells, and are often arranged in layers around them. The histological source for these cells was supposed to be the leucocyte by Schueppel, Ziegler, and Treves; the endothelial cells of the lymph-spaces by Aufrecht, Hering, and Woodward; the endothelial cells of the blood-vessels and lymphatics or connective-tissue cells by Rindfleisch and nearly all of the modern authors. The endothelioid cells represent the embryonal cells, the product of proliferation from any of the fixed tissue-cells in a tubercular lesion, and they remain as such until they are destroyed by degenerative changes from the continued action upon them of the bacillus of tuberculosis or its ptomaines, or until, on cessation of the primary cause, they are transformed into tissue of greater durability.

Reticulum.—Schueppel first called attention to the reticulated structure of tubercle by his description of the reticular arrangement within tubercles of lymphatic glands.

The reticulum, according to most authors, consists of the pre-existing connective tissue pushed asunder by the new cells. According to Wagner, Schueppel, Brodowski, Thaon, and Ziegler, it is made up of protoplasm. Buhl taught that the giant and epithelioid cells secrete a substance at their periphery which, on becoming firm, is formed into a structure resembling connective tissue. According to his researches only the marginal zone is supplied with loose, ready-formed, connective tissue of the organ. Wahlberg maintained that the principal reticulum consists of protoplasm which is traversed by a net-work of connective tissue. The reticulum is always more marked in the periphery of the tubercle-nodule, where, from pressure, it is condensed into a fibrous capsule (Fig. 98, C).

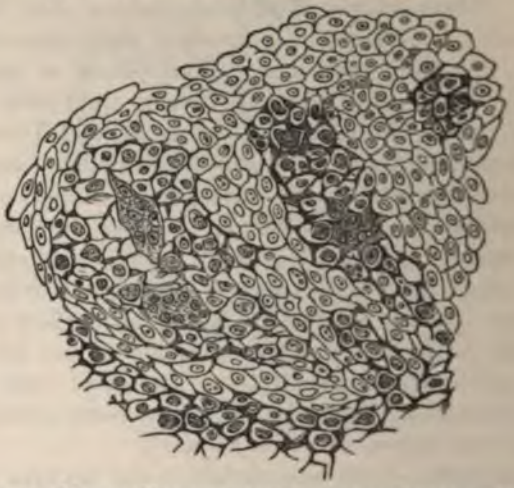

FIG. 97.—SECTION FROM MUCOUS MEMBRANE OF PHARYNX, SHOWING EPITHELIOID CELLS WITH A FEW SMALL GIANT CELLS. × 350. (*Birch-Hirschfeld.*)

Arrangement of the Cells in a Recent Tubercle-Nodule.—The earliest evidence of the formation of a tubercle-nodule, as witnessed under the microscope, is the appearance of small cells which resemble ordinary embryonal cells, which are the product of tissue proliferation from a mesoblastic matrix, usually the connective tissue, and its embryological and histological prototype, the endothelial cells of blood-vessels and lymphatics. From these cells the epithelioid and giant cells are, later, developed. Some of the central cells, by appropriation of a superabundance of food furnished by leucocytes in a state of fragmentation, become hyperplastic, and are transformed into giant cells; these occupy the centre of the nodule. Around these cells the smaller or epithelioid cells arrange themselves, and between them and in the periphery of the nodule are found the smallest cells,—the leucocytes.

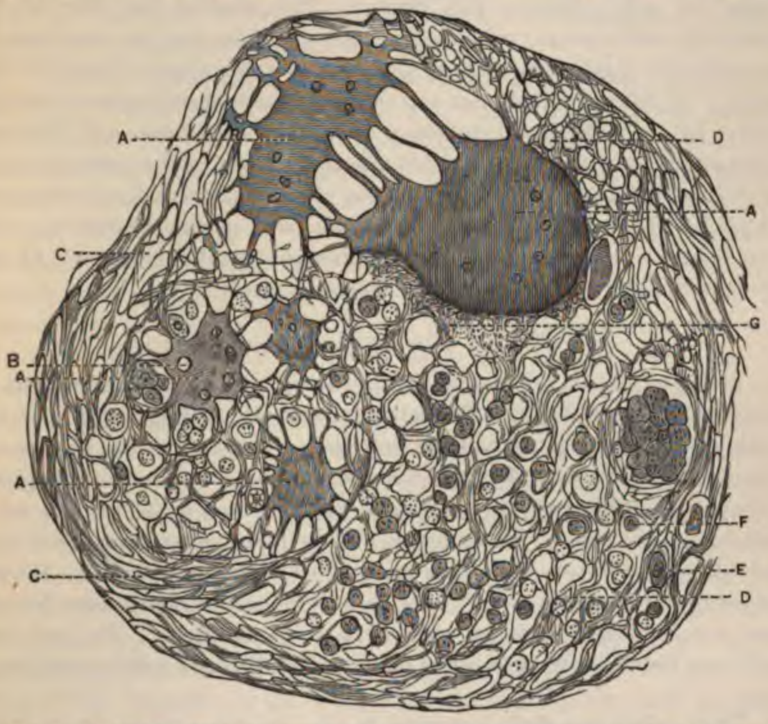

FIG. 98.—FULLY-DEVELOPED RETICULAR TUBERCLE OF LUNG. × 450. (*Hamilton.*)

A, A, A, giant cells; B, vacuole in one of these; C, peripheral capsule of fibrous tissue; D, reticulum of the tubercle; E, large endothelium-like cells lying on the reticulum and within its meshes; F, smaller "lymphoid" cells occupying the same situation; G, peripheral fibrous-looking border of the giant cells.

Gaule and Tizzoni distinguish three zones in a tubercle: (1) an external, composed of small round cells; (2) a leper, epithelial, or middle zone, containing the reticulum; (3) a central space containing a giant cell. The structure of a tubercle is not always typical, and hence the division into zones is based more on theoretical grounds than actual observation. The giant cell is not an essential histological element of tubercle, but an accidental product. In some tubercles giant cells cannot be found, while in others they are numerous. Giant cells can only develop from epithelioid cells if the local conditions are favorable for hypernutrition; that is, if the leucocytes in a condition of fragmentation are within their reach. If they are present they always mark the location of the starting-point of the tubercular infection, as only the older epithelioid cells undergo this change. The number and size of the epithelioid cells are also subject to great variation, and are modified by the nutritive conditions within and in the immediate vicinity of the nodule. If cell proliferation is active the epithelioid cells appear densely packed in the reticulum, nutrition is greatly impaired, and the new cells undergo degenerative changes before they attain their average size. The leucocytes are scattered among the giant and epithelioid cells, and, as they reach the part through the inflamed wall of the capillaries in the immediate vicinity, they are most numerous in the periphery of the nodule and along the course of the affected vessels.

GROWTH OF THE TUBERCLE-NODULES.

The typical tubercle-nodule is microscopic in size. The growth of the swelling depends on the formation of new tissue, migration of leucocytes, and confluence of nodules into larger masses. The bacillus of tuberculosis, when brought in contact with fixed tissue-cells susceptible to its pathogenic action, incites tissue proliferation, which always takes place by karyokinesis. Baumgarten's investigations leave no doubt that phatycytes constitute the entire mass of the forming tubercle. He has also observed karyokinetic figures in tubercular tissue in cells derived from the connective tissue, endothelia, and epithelia. The tubercle bacilli are found in the interior of giant and epithelioid cells and between them.

Each tubercle-nodule increases in size by the growth of new cells from pre-existing tissue, and as the primary cause, the bacillus of tuberculosis, multiplies in the tissues, bacilli are conveyed into the surrounding tissues by leucocytes or the plasma-current, and new centres for tubercle formation are established, which, later, become confluent, forming masses of considerable size, the numerous foci of caseation corresponding to the centre of a nodule. The growth of tubercle is favored by local and general conditions which diminish tissue resistance, while retardation takes place in consequence of degenerative changes in the cells of which it is composed, or, if the cells are converted into tissue of a higher type, from disappearance or suspension of activity of the primary cause.

PATHOLOGICAL VARIETIES OF TUBERCLE.

Several varieties of tubercle have been described, according to the histological structure of the tubercle or the structure or condition of the cells of which it is composed.

Reticulated Tubercle.—This is the ordinary form of tubercle usually met with, and the most important anatomical feature is the presence of a well-defined reticulum, composed of pre-existing connective tissue and a delicate net-work of branching giant cells, in the meshes of which are found the epithelioid cells and leucocytes.

Fibrous Tubercle.—In contradistinction to the reticulated or lymphoid tubercle, a few years ago the fibrous tubercle was described, distinguished by its pearl-like, light-gray appearance, but possessing the same inherent tendency to caseation. It is said to be found most frequently in dense, fibrous tissue, and quite often in newly-formed connective tissue. Histologically it is composed of nodules of dense connective tissue, the cells of which have undergone rapid growth, containing, frequently, more than one nucleus. A further development only takes place in the interior of the nodule, as here caseation occurs, the caseous focus being surrounded by a firm capsule of connective tissue. The description of fibrous tubercle by Langhans differs materially from the above. According to investigations of this author, the fibrous tubercle has for its favorite location the so-called parenchymatous organs, as the lungs, liver, spleen, kidneys, testicles, epididymis, and brain. The larger nodules are composed of three zones. The central zone consists of a few connective-tissue fibres, free oil-globules, and cells in a condition of fatty infiltration. The middle zone is composed of connective tissue. As the cells of this zone are not numerous, it presents the appearance of a capsule; in reality, however, it is not a capsule in the proper sense of the word, but a matrix of tissue proliferation, from which the central part of the tubercle is the offspring. Both Langhans and Schueppel, like nearly all of the modern pathologists, regard fibrous tubercle not as a distinct special anatomical form, but as an ordinary tubercle in which the epithelioid cells in the peripheral zone have been converted into connective tissue. Fibrous tubercle differs from the ordinary cellular variety only in so far that it contains a larger amount of connective tissue. If in a tubercle-nodule at the time the young cells are yet vigorous the primary microbic cause ceases to act, degenerative changes fail to take place and the embryonal cells are transformed into connective tissue. The cicatricial condition starves out remaining embryonal cells; at the same time an impermeable wall of connective tissue is thrown around the primary depot of infection, which effectually guards against the escape of active bacilli or their spores into the surrounding tissues.

Hyaline Tubercle.—Chiari described another variety of tubercle—the hyaline tubercle. The first specimen in which he found this variety was taken from the liver of a tuberculous child 4 years of age. The nodules in the brain, lungs, and bronchial glands in the same case presented the ordinary structure of lymphoid tubercle. The clear hyaline structure of those found in the liver gave them a very peculiar appearance. The change is believed to be due to a hyaline degeneration of the reticulum, and resembles most closely the hyaline degeneration of the capillaries of the brain. Chiari conjectures that it may be regarded as a benign change opposed to caseation, which tends to infection. Hyaline degeneration of any pathological product must now be considered as one of the earliest phases of coagulation necrosis, and, if a considerable area of the nodule undergo this change rapidly and simultaneously, the structures will present a hyaline appearance; but if the hyaline product continue to be acted upon by the same causes, caseation will follow, and the hyaline tubercle becomes a cheesy tubercle.

CASEATION.

The gray or miliary tubercle is transformed into the yellow, crude, or cheesy tubercle by a process which is called caseation, or tyrosis. The exact nature of this process remains unknown. The cheesy material is composed of the products of cell necrosis. Early death of cells is the most characteristic pathological feature of tubercle, which distinguishes it from all other forms of chronic inflammation. Two causes can be advanced to explain this peculiar and almost pathognomonic form of degeneration, which occurs, almost without exception, in every tubercle if a sufficient length of time has elapsed: 1. Inadequate blood-supply. 2. Specific action of the bacillus of tuberculosis or its ptomaines. Caseation always commences in the centre of a nodule, consequently at a point most remote from the vascular supply, and in cells which have been exposed longest to the deleterious effect of the primary microbic cause. Tubercle is a non-vascular product. From causes which, as yet, are not known, the tubercular product is not supplied with new blood-vessels. The angioblasts are transformed into epithelioid cells that have lost their power of vessel formation. Nodules which have primarily an intra-vascular origin are rendered avascular by closure of the vessel from intra- and peri- vascular cell proliferation. If the primary starting-point is outside of the vessels, the rapidly accumulating cells exert pressure upon the surrounding vessels, and thus diminish the blood-supply to the part affected. The new cells require an adequate blood-supply for their further development, and if this fail to take place, as is the case in every tubercular product, they necessarily suffer from malnutrition, and undergo degenerative changes at an early stage of their existence. A deficient blood-supply, in the absence of other causes, would result in fatty degeneration of the new vessels; but caseation is something different from ordinary fatty degeneration, and the bacillus of tuberculosis, or its ptomaines, must be regarded as its immediate and essential cause. Caseation is preceded by coagulation necrosis, which is one of the results of the specific action of the bacillus on the tissues. The coagulation necrosis commences in the giant cells, and in the epithelioid cells in the centre of the nodule, and caseation follows as soon as the dead cells have lost their histological identity, and appear under the microscope as a *débris* in which no distinct cell forms can be identified. Caseation is attended by softening, which can be readily recognized in tubercular masses the size of a hazel-nut to that of a walnut, composed of numerous confluent nodules with as many caseating foci.

In such masses the small, cheesy cavities become confluent and form spaces of considerable size. Caseation proceeds from the centre of each nodule toward the periphery, layer after layer of epithelioid cells being destroyed and changed into cheesy material. The part of a tubercle-nodule which has undergone caseation contains few, or no, bacilli, and yet inoculation experiments show it to be highly infectious. The cheesy material does not furnish the proper nutrient material for the growth and development of the bacillus, which dies from starvation, while the spores, being more durable and possessing greater power of resistance, remain in an active condition for an indefinite period of time in the dead material, and it is due to their presence that infection takes place from cheesy foci, and that successful inoculations can be made with cheesy material. While the disease has become arrested in the centre of a nodule, with the appearance of caseation, its growth in a peripheral direction pursues the same relentless course. The bacilli multiply in recent tubercular tissues, and are carried beyond the peripheral zone into the surrounding tissues, where new, independent foci of infection are thus established, which, in the course of time, pass through the same series of pathological changes as the primary nodules. It is a well-known clinical fact that acute miliary tuberculosis is not a primary affection, as in all such cases a careful post-mortem examination will reveal the presence of a cheesy focus in a lymphatic gland, the lungs, testicles, a joint, or bone, or some other organ, from which the infection occurred. Weber found cheesy foci in 16 cases of tuberculosis of serous membranes. The cheesy mass may lie latent so long as it is solid, but as soon as it liquefies the spores which it contains can be taken up by the blood-vessels and prove a cause of general infection.

CALCIFICATION.

One of nature's means in preventing the local extension of tubercle and in guarding against regional and general infection is calcification of the tubercular product. This can only occur as a secondary condition in tubercles that have undergone caseation. Calcification implies the removal of the cheesy material and the substitution for it of inorganic, calcareous material. It is a process which greatly resembles petrifaction. Arrest of the tubercular process by caseation and calcification frequently takes place in the lungs, and, occasionally, in the lymphatic glands.

CHAPTER XVIII.

CLINICAL FORMS OF SURGICAL TUBERCULOSIS.

IT is but a few years since it was thought impossible that any other organ than the lungs should be the seat of tuberculosis. The different forms of surgical tuberculosis that will be described below were not correctly understood until quite recently, and consequently a rational surgical treatment was out of question. Most all of the localized tubercular processes were included under the general term *scrofula*, and were regarded as local manifestations of a general dyscrasia, and treated in accordance with this view of their pathology. The discovery of the bacillus of tuberculosis has rendered the word scrofula obsolete, and has assigned to the tubercular processes in the various organs and tissues of the body their correct etiological and pathological significance, and paved the way for their successful surgical treatment. There is hardly a tissue in the body which may not become the primary seat of tubercular infection, or which escapes when diffuse dissemination occurs through the medium of the general circulation. The frequency of tubercular affections is something appalling. At least 1 person out of every 7 dies of some form of tuberculosis. Most of the large hospitals contain from 25 to 50 per cent. of patients afflicted with this disease. The ravages of the disease are to be seen everywhere, in the shape of disfiguring scars of the neck, deformed limbs, and bent spines. Health resorts, frequented for years by tubercular patients, have become infected to such an extent that there is great danger of the whole population becoming exterminated by this disease. The sources of infection in such places have become so numerous that it is unsafe to breathe the air, to drink the water, or to eat the food prepared in houses which for years have been hot-beds for the bacillus of tuberculosis, and by persons carrying the microbe upon every square inch of their surface. That whole communities and nations, where this disease has been prevalent for centuries, have not been completely depopulated long ago is owing to the fact that many persons possess, from the time of their birth, a degree of resistance to infection that even direct infection by inoculation would prove harmless. The bacillus is not the sole, but the essential, cause of tuberculosis.

HEREDITARY AND ACQUIRED PREDISPOSITION.

Almost every author recognizes, as an important element in the etiology of tuberculosis, the existence of a hereditary or acquired predisposition. Little is known in reference to the real nature of such a predisposition. A weakness of the lymphatic vessels in scrofulosis was recognized by Sylvius as early as 1695, by Portal in 1690, and still later by Bell, Percival Pott, Hufeland, and Broussais. Fox is of the opinion that a disposition to tuberculosis is created by certain anatomical or physiological defects in the lymphatic system. The cause of scrofula was ascribed by Virchow to a weakness or imperfection in the arrangement of the lymphatic system; by Hueter to a dilatation of lymph-spaces; and by Billroth to a constitutional anomaly. Mordhorst regards a sluggish circulation, the consequence of superficial, imperfect respiration, by causing capillary stasis and favoring inflammatory exudation, a potent factor in producing that peculiar vulnerability of the tissues in scrofulous subjects. Rokitansky placed great stress on the importance of an imperfect circulatory and respiratory apparatus as a predisposing cause of tuberculosis. In 1871 Friedländer suggested that in cases of tuberculosis there might be present, and active, a fusion of the scrofulous and tubercular diathesis,—a view which was indorsed by Charcot in 1877. Aufrecht claims that the disposition to the origin of tubercle may be found in the lymphatic vessels. Riedel defines the hereditary predisposition to tuberculosis as consisting in a peculiar defect in the anatomical arrangement of the tissues, especially of the lymphatic glands, which furnish a favorable soil for infection. Schüller believes that the noxæ of tuberculosis excite a slow form of inflammation, with a tendency to speedy retrograde metamorphosis of the new material. Quincke recognized a close relationship between scrofula and tuberculosis, when he says: "Scrofulous persons are especially predisposed to tuberculosis; tuberculosis hardly ever occurs except in scrofulous persons." Ziegler was aware that pulmonary phthisis is the most frequent cause of death in scrofulous patients. Whittier, in comparing the etiology of tuberculosis with syphilis, makes use of the following very positive language:—

"There is no such a thing as a predisposition to either disease. Either a man has syphilis, or he has it not. One man is not more predisposed to either disease than another. Syphilis affects one individual more than another because its virus finds a better lodgment upon mucous membrane. Tuberculosis finds, also, fortuitously, a better *nidus* in one case than another. The virus of tuberculosis is lodged, in one case, and not coughed up, just as in syphilis the virus is secreted and not washed off." And again: "From any chancre, plaque, gumma, or other deposit of syphilis, re-absorption may take place at any time, and re-infection with syphilis; or, better, re-appearance of external signs. So from any caseous nodule, wherein the tuberculous virus is locked up in temporary innocence, absorption may take place under favoring circumstances, and a new outbreak of tuberculous symptoms appear, the quantity of virus thus set free determining, to a great extent, perhaps, the virulence of the symptoms. While the virus is thus locked up, the disease is latent; when set free, it is manifest." Wynne Foot says: "Tubercles are small-celled overgrowths of lymphatic tissue that have preserved such uniformity of size, color, and shape as to have long suggested the probability of their lymphatic origin." Wilson Fox regarded tubercle as an overgrowth or hyperplasia of lymphatic tissue resulting from irritation of the lymphatic elements.

Savory, in speaking of the relation of scrofula to tubercle, remarks: "It appears to me that there is nothing sufficient to warrant the pathological distinction which it is now the fashion to make between scrofula and tubercle." And further: "Tubercle may be said to be the essential element of scrofula." According to Rokitansky, the most frequent seat of tubercle in children is in the lymphatic glands. Virchow maintained that scrofula constitutes the basis of tubercle, and that in man tuberculosis depends in general on scrofula. He asserts, further: "On account of the histological identity of the scrofulous and tubercular new growths, it is often impossible, in a given tubercular lesion, to determine how much is inflammatory and how much is tubercular." From the above quotations it becomes apparent that nearly all of the older authors recognized, if not the identity, at least a close relationship between scrofula and tuberculosis. The identity of scrofula and tuberculosis was established not upon anatomical or pathological researches, but was definitely settled by the discovery of the same cause in the local lesions of both. The demonstration of any definite anatomical defect, hereditary or acquired, which acts as a predisposing cause to tubercular infection, has so far not succeeded. Only a few years ago Formad made some interesting studies concerning the histological structures of tissues that are known to be prone to tubercular infection, and he believed that the changes constantly found were such that favored the arrest of migrating cells. It is more probable that the hereditary or acquired predisposition to tuberculosis, which must now be recognized as an important element in the causation of the disease, must be regarded rather as a diminution of the power of resistance inherent in the tissues to the action of the specific microbic cause than any characteristic anatomical cell defects. From a clinical stand-point, it is important to remember that in the causation of tuberculosis we must recognize a combination observation. The giant cell is not an essential histological element of tubercle, but an accidental product. In some tubercles giant cells cannot be found, while in others they are numerous. Giant cells can only develop from epithelioid cells if the local conditions are favorable for hypernutrition; that is, if the leucocytes in a condition of fragmentation are within their reach. If they are present they always mark the location of the starting-point of the tubercular infection, as only the older epithelioid cells undergo this change. The number and size of the epithelioid cells are also subject to great variation, and are modified by the nutritive conditions within and in the immediate vicinity of the nodule. If cell proliferation is active the epithelioid cells appear densely packed in the reticulum, nutrition is greatly impaired, and the new cells undergo degenerative changes before they attain their average size. The leucocytes are scattered among the giant and epithelioid cells, and, as they reach the part through the inflamed wall of the capillaries in the immediate vicinity, they are most numerous in the periphery of the nodule and along the course of the affected vessels.

GROWTH OF THE TUBERCLE-NODULES.

The typical tubercle-nodule is microscopic in size. The growth of the swelling depends on the formation of new tissue, migration of leucocytes, and confluence of nodules into larger masses. The bacillus of tuberculosis, when brought in contact with fixed tissue-cells susceptible to its pathogenic action, incites tissue proliferation, which always takes place by karyokinesis. Baumgarten's investigations leave no doubt that phatycytes constitute the entire mass of the forming tubercle. He has also observed karyokinetic figures in tubercular tissue in cells derived from the connective tissue, endothelia, and epithelia. The tubercle bacilli are found in the interior of giant and epithelioid cells and between them.

Each tubercle-nodule increases in size by the growth of new cells from pre-existing tissue, and as the primary cause, the bacillus of tuberculosis, multiplies in the tissues, bacilli are conveyed into the surrounding tissues by leucocytes or the plasma-current, and new centres for tubercle formation are established, which, later, become confluent, forming masses of considerable size, the numerous foci of caseation corresponding to the centre of a nodule. The growth of tubercle is favored by local and general conditions which diminish tissue resistance, while retardation takes place in consequence of degenerative changes in the cells of which it is composed, or, if the cells are converted into tissue of a higher type, from disappearance or suspension of activity of the primary cause.

PATHOLOGICAL VARIETIES OF TUBERCLE.

Several varieties of tubercle have been described, according to the histological structure of the tubercle or the structure or condition of the cells of which it is composed.

Reticulated Tubercle.—This is the ordinary form of tubercle usually met with, and the most important anatomical feature is the presence of a well-defined reticulum, composed of pre-existing connective tissue and a delicate net-work of branching giant cells, in the meshes of which are found the epithelioid cells and leucocytes.

Fibrous Tubercle.—In contradistinction to the reticulated or lymphoid tubercle, a few years ago the fibrous tubercle was described, distinguished by its pearl-like, light-gray appearance, but possessing the same inherent tendency to caseation. It is said to be found most frequently in dense, fibrous tissue, and quite often in newly-formed connective tissue. Histologically it is composed of nodules of dense connective tissue, the cells of which have undergone rapid growth, containing, frequently, more than one nucleus. A further development only takes place in the interior of the nodule, as here caseation occurs, the caseous focus being surrounded by a firm capsule of connective tissue. The description of fibrous tubercle by Langhans differs materially from the above. According to investigations of this author, the fibrous tubercle has for its favorite location the so-called parenchymatous organs, as the lungs, liver, spleen, kidneys, testicles, epididymis, and brain. The larger nodules are composed of three zones. The central zone consists of a few connective-tissue fibres, free oil-globules, and cells in a condition of fatty infiltration. The middle zone is composed of connective tissue. As the cells of this zone are not numerous, it presents the appearance of a capsule; in reality, however, it is not a capsule in the proper sense of the word, but a matrix of tissue proliferation, from which the central part of the tubercle is the offspring. Both Langhans and Schueppel, like nearly all of the modern pathologists, regard fibrous tubercle not as a distinct special anatomical form, but as an ordinary tubercle in which the epithelioid cells in the peripheral zone have been converted into connective tissue. Fibrous tubercle differs from the ordinary cellular variety only in so far that it contains a larger amount of connective tissue. If in a tubercle-nodule at the time the young cells are yet vigorous the primary microbic cause ceases to act, degenerative changes fail to take place and the embryonal cells are transformed into connective tissue. The cicatricial condition starves out remaining embryonal cells; at the same time an impermeable wall of connective tissue is thrown around the primary depot of infection, which effectually guards against the escape of active bacilli or their spores into the surrounding tissues.

taneous discharge or after incision, the superficial granulations are destroyed by the suppurative process which is initiated, exposing the patient to the additional risks of septic infection and a more rapid local and general dissemination of the tubercular process.

Symptoms and Diagnosis.—The tubercular abscess is called a cold abscess because it lacks the characteristic clinical phenomena which attend the development of an acute or hot abscess. There is but little, if any, rise of the local temperature, and, unless the abscess has reached the skin, looks rather preternaturally pale than red, and the abscess itself is always painless and not tender on pressure. The pain, if present, is referred to the primary seat of the tubercular inflammation. Fluctuation is usually well marked, as the tissues around the abscess are not much infiltrated. The most important clinical feature of a cold abscess is its tendency to wander from the place where it originated to distant localities by gravitation; hence the name given to it by German writers, *senkungs abscess*. Thus, in tubercular spondylitis, the abscess may appear in the lumbar region, and is then called *lumbar abscess;* it may follow the iliac muscle and appear in one of the iliac regions, and is then called *iliac abscess;* or, finally, it may follow the psoas muscle and appear above or below Poupart's ligament, when it constitutes a *psoas abscess.*

In tuberculosis of the hip-joint the abscess appears posteriorly underneath the gluteal muscles, if perforation of the capsule in this direction take place; or it appears anteriorly a considerable distance below the hip-joint, if perforation of the capsule take place in an opposite direction. As the contents of the abscess carry the original cause of the disease, infection of the tissues takes place along the whole course of the abscess, which is always lined with infected granulation tissue. Although the primary cause of a tubercular abscess is most frequently a tuberculosis of a joint or bone, it can also develop in the course of any localized form of tuberculosis, and it is quite frequently met in the course of tuberculosis of the lymphatic glands. The diagnosis must be made with special reference to the nature and location of the primary lesion. In tuberculosis of the spine the fixed pain in the region of the affected vertebræ, radiating from here in the direction of the nerves on each side, is an important symptom, and this symptom is always aggravated by flexion and ameliorated by extension of the spine. In coxitis the pain in the beginning of the disease is usually referred to the inner aspect of the knee-joint, but is always increased by motion in the hip-joint. In cold abscess, caused by glandular tuberculosis, the clinical history will point to a chronic inflammation of the glands which preceded the formation of the abscess. As soon as the abscess reaches the skin that structure becomes inflamed, red, and more and more attenuated by pressure and inflammation, until spontaneous perforation takes place at a point subjected to greatest pressure. If a tubercular product become the seat of a secondary infection with pus-microbes, the subsequent symptoms, local and general, are those of suppurative inflammation. The temperature, which was normal, or nearly so, increases and presents the daily curves indicative of suppuration, while the abscess, which has been painless heretofore, becomes painful and tender on pressure; in fact, a chronic inflammation has been supplanted by an acute one, with a corresponding change of the clinical picture. If any doubt remain as to the character of the swelling and the nature of its contents, this can be dispelled at once by resorting to an exploratory puncture. In cold abscess the fluid removed presents the appearance of serum in which minute particles of broken-down tissues are suspended, while in an abscess caused by a mixed infection it presents the macroscopical and microscopical appearances of pus.

Prognosis.—The danger attending tubercular abscess must be estimated exclusively by the extent and location of the primary disease and the presence or absence of tuberculosis in other organs. If the general health remain unimpaired, even an extensive local tubercular disease may be amenable to a spontaneous cure or successful surgical treatment. On the other hand, a tubercular abscess developing in the course of an insignificant and unimportant local lesion occurring in an anæmic person, the subject of incipient multiple foci in different organs, must be regarded as a formidable condition, with little or no prospects of a favorable termination. *I have learned to regard pronounced anæmia as an unfavorable symptom in the different forms of surgical tuberculosis, as it is often an expression that general infection has occurred.* Another important matter to be taken into consideration, in making a prognosis in cases where general infection can be excluded, is the possibility of eradicating the primary lesion by operative interference. Where this can be done, the chances of successful treatment of the local disease are much better; at the same time, the removal of all the infected tissues is the best guarantee against general infection. Other things being equal, the prognosis is better in patients without a hereditary history of tuberculosis, and in young persons than those advanced in years.

Treatment.—The surgical treatment of large tubercular abscesses is always fraught with danger from the fact that, even if conducted under strict antiseptic precautions, it is not always possible to prevent infection with pus-microbes. Large tubercular abscesses were a "*nole me tangere*" to the older surgeons, as it was well known evacuation by incision would be followed within a few days by hectic fever, profuse sweating, diarrhœa, and other symptoms of septic infection. The early advocates of the antiseptic treatment hoped that the time had come when the surgeon had it in his power to prevent septic infection during the operation by resorting to the necessary antiseptic precautions, and to maintain an aseptic condition throughout the after-treatment under an efficient antiseptic hygroscopic occlusive dressing. If we remember that in cases where the abscess originated from a primary lesion inaccessible to direct treatment it may require months for the healing process to be completed, it is not surprising that even the strictest antiseptic precautions in the hands of the ablest surgeons have failed in protecting the abscess-cavity against septic infection for such a long time.

In a number of tubercular abscesses originating from a tubercular focus in the vertebra, in the hip- and knee-joints, I have succeeded in preventing infection, and the patients were cured after several months of the most careful and watchful treatment; but in a greater number of cases infection occurred at the time of operation, or weeks or months later during change of the dressing, or in consequence of a slipping of the dressing. In abscesses in the gluteal or inguinal regions, especially in children treated by incision and drainage, it is almost next to impossible to maintain an aseptic condition for weeks and months, and the most careful and laborious efforts in this direction will often result in failure.

(a) Evacuation by Aspiration followed by Antiseptic Irrigation and Subcutaneous Iodoformization.—The frequency with which failures have occurred after incision and drainage, in the hands of the most enthusiastic followers of the antiseptic treatment, has again aroused the fear of surgeons in attacking large tubercular abscesses by incision and drainage, and the subcutaneous evacuation with subsequent disinfection of the abscess-cavity has again come into favor. That iodoform exerts an inhibitory effect on the growth of the bacillus of tuberculosis is now generally accepted. Its use in the treatment of tubercular affections is almost universal. It has been extensively used for injection into tubercular abscess, after evacuation by aspiration, since Bruns advocated this treatment, in 1887. It was first used dissolved in ether in the proportion of 1 part to 20. The ethereal solution has the advantage of bringing the drug in contact with every part of the interior of the cavity by the distention which takes place from the expansion of the ether when exposed to the body-temperature, but the injection is usually followed by considerable pain. Bruns used a suspension of iodoform in glycerin and alcohol. Recently the following formula was suggested by Krause:—

Iodoformi subt. pulveris,	50.0
Mucil. gummi arab.,	23.0
Glycerini,	83.0
Aquæ destillatæ, q. s. ad	500.0

(Ten-per-cent. iodoform mixture.)

The evacuation of the abscess is to be done with an ordinary trocar under strict antiseptic precautions. The surface of the abscess is thoroughly disinfected in the usual manner, and the instruments rendered aseptic by boiling. The trocar is inserted in such a manner that a track, at least an inch in length, is made underneath the skin before the instrument is plunged into the abscess-cavity, in order to make the wound, after the removal of the instrument, as nearly as possible subcutaneous. As tubercular abscesses usually contain shreds of dead connective tissue and masses of broken-down granulation tissue, the evacuation is often attended by a considerable difficulty, as these substances block the opening of the instrument and thus prevent evacuation. The simplest procedure to overcome these difficulties is to introduce through the canula a small hook made by bending an aseptic wire, and to extract with it any substance which interferes with the escape of the fluid contents. Gentle, uniform pressure is of great value in expediting the escape of the contents and in preventing the entrance of air. Iodoformization of the abscess-cavity is not to be done until complete evacuation of solid detached particles has been effected by means of irrigation with a 3-per-cent. solution of boracic acid. This can be readily done by inserting the glass tip of an irrigator which holds the solution into the canula. A sufficient quantity of fluid is allowed to flow into the cavity until this is distended as much as before the evacuation of the fluid, when, by gentle pressure, it is forced out through the canula. By filling and emptying the cavity alternately in this manner a requisite number of times, complete evacuation of the fluid and loose solid contents is effected, and the cavity is now ready for iodoformization. Whatever formula for the solution is selected, not more than half a drachm of the iodoform should be injected at the first time, and in children even less. If this dose does not produce any unpleasant symptoms, it may be increased the next time the operation is repeated. There seems to be very slight danger of iodoform intoxication, not even a symptom of this being observed in 109 cases thus treated by Bruns, of Tübingen. The injection is made with an ordinary but perfectly aseptic syringe, the nozzle of which must fit accurately into the outer end of the canula. If the ethereal solution is used, the iodoform will become diffused over the entire inner surface of the abscess-cavity; but if a non-evaporating medium for the mixture is used, this must be done by gently kneading and rubbing the parts over the abscess after the canula is withdrawn. The injection containing the iodoform is, of course, intended to remain in the cavity. The puncture in the skin is closed with collodium, and the walls of the abscess are kept in contact by compress and bandage. Absolute rest is to be enforced for some time by splints or confinement in bed, according to the location of the abscess. The operation is to be repeated in the course of a week, or as soon as the abscess-cavity has partially refilled. The treatment of tubercular abscesses by subcutaneous evacuation, with subsequent iodoformization, should be adopted and repeated, from time to time, in all cases where the primary lesion is inaccessible to radical surgical treatment, and may yield good results in cases which heretofore had been subjected to heroic surgical treatment from the beginning. It may also prove useful as a preparatory treatment in cases which subsequently require operative treatment.

(b) **Incision and Removal of Primary Focus.**—In all cases where, from the anatomical location of the primary lesion, it is possible to remove the tubercular product by operative interference, and the patient is free from other tubercular affections, a radical operation is absolutely indicated. In such cases the abscess-cavity is laid freely open in a direction which will secure most ready access to its interior with least injury to surrounding parts. After the abscess has been opened, its contents are washed away by irrigating with an aqueous solution of iodine, after which the granulations lining the cavity are scraped out with a sharp spoon, and the primary lesion is removed in a similar manner. In dealing with such cavities it is important not to forget that the granulations contain tubercle bacilli, and, if they are not thoroughly removed, the principal object of the operation—removal of the primary cause—has not been accomplished, and a return of the disease is to be expected. If the abscess communicates with a primary focus in the bone, it is advisable to resort to ignipuncture of the bone after the cavity has been cleared of the granulations with the sharp spoon. The wound is to be closed in the usual manner, leaving only a small opening at the most dependent point for drainage. The scraped surfaces are now in the same conditions for primary union as a recent aseptic wound, and, if kept in accurate apposition by the antiseptic dressing, which answers at the same time the purpose of a compress, primary union throughout is frequently obtained. Abscesses which have opened spontaneously, or during the treatment of which infection has occurred, must be treated on the same principles as acute abscesses. As far as can be done, the suppurating granulations should be removed with the sharp spoon and efficient tubular drainage established, and by frequent antiseptic irrigations an attempt is made to prevent septic infection. Landerer has recently called attention to the value of balsam of Peru in the treatment of tubercular affections. He claims that this drug acts beneficially by stimulating the tissues to renewed activity, thus neutralizing, at least to a certain degree, the pathogenic effect of the bacilli. Sayre, of New York, has used this remedy for more than thirty years in the treatment of tubercular joints, and his results have certainly been extremely satisfactory. In the treatment of open, suppurating, tubercular cavities, the balsam of Peru should be tried as a local application. As a fluid for irrigation under the same circumstances, nothing can surpass the efficacy of a strong aqueous solution of tincture of iodine.

(c) **General Treatment.**—Patients suffering from suppurating tubercular cavities require nutritious food, ale, porter, or some of the substantial wines; out-door air will often prove the best tonic. Change of residence to the sea-shore or some mountain resort has often been known to effect a cure when recovery was despaired of as long as the patients lived in localities less favorably located. In the way of medication the treatment must be purely symptomatic. Appetite is restored by the use of bitter tonics; anæmia is treated by the administration of some mild preparation of iron, as the syrup of iodide of iron, tincture of chloride of iron, albuminate of iron, or citrate of iron. If codliver-oil is given it should be administered pure, and not in emulsion, and never upon an empty stomach. The pale Norwegian oil is the best. The best time to give the oil, without disturbing the digestion, is an hour or an hour and a half after each meal, in doses of from a teaspoonful to a tablespoonful, according to the condition of the digestion and the age of the patient.

TUBERCULOSIS OF THE INTERNAL EAR.

That an ordinary otitis media with perforation of the tympanum may occasionally be transformed into a tubercular lesion by the entrance of tubercle bacilli there can be no doubt. Habermann has recently investigated this subject by examining, post-mortem, 18 tuberculous subjects, in whom either otorrhœa or deafness, without active discharge, had been observed during life, and in 9 of these he could demonstrate the presence of tubercular lesions in the auditory canal. In 1 case he found, in the left auditory apparatus, tuberculosis of the entire middle ear where the tympanum was intact. In another tubercular subject, a man 38 years of age, in whom tuberculosis of the ear was observed a year and a half before death, the post-mortem revealed extensive tuberculosis of the cochlea, in the internal auditory canal, and in the superior semicircular canal, while the other semicircular canals and the vestibule were destroyed by caries. Infection with the bacillus tuberculosis of granulations in the middle ear through a perforation in the tympanum can occur in persons otherwise in perfect health. The diagnosis in such cases can be readily made by removing fragments of granulation tissue for microscopic examination. If they are found to contain tubercle bacilli a positive diagnosis has been made, and no time should be lost in resorting to a radical operation. The removal of the infected granulations with a sharp spoon, followed by irrigation with a warm 3-per-cent. solution of boric acid and iodoformization of the cavity, are the measures to be employed in removing the infected focus and in preventing extension of the disease into other parts of the ear, the mastoid cells, or the meninges of the brain.

TUBERCULOSIS OF THE IRIS.

Inoculations of the anterior chamber of the eye with tubercular material have shown the extreme susceptibility of the iris to tubercular infection. That this structure should occasionally become the seat of primary infection is evident from a case recently reported by Griffith. The patient was a female child 7 months old. The eye had been affected for one month; there was an enlarged gland in the neck on the same side, but there were no other physical signs of tubercle; no history of heredity. A yellowish nodule grew from the periphery of the iris of the right eye, and numerous millet-seed-like bodies from its surface; the pupil was closed, but there was no acute inflammation. The local disease increased rapidly in extent. The eye was enucleated after three weeks' treatment. The disease was found to be confined to the iris and ciliary body. Under the microscope the new growth showed the characteristic structure of tubercle. In 32 recorded cases, in which microscopic and bacteriological tests left no doubt as to the tubercular nature of the disease, only 1 eye was affected in 29. The average age of the patients was 12 years; youngest 4 months, oldest 51 years. In 10 cases bacilli was searched for, but only found in 4; in 1 of the remaining 6 cases, however, the inoculation test was successful. A number of patients recovered completely and permanently after enucleation.

If the tubercle is located on the anterior surface of the iris, a diagnosis can usually be made without much difficulty at an early stage, as the inflammatory product can be seen and carefully examined through the transparent cornea. If some doubt exist at first as to the nature of the swelling, this is soon set aside by the progress of the disease. The primary nodule soon becomes surrounded and covered by an eruption of miliary tubercles. The disease here, as elsewhere, shows its characteristic clinical feature,—progressive extension, affecting all the structures contiguous to or continuous with the part primarily affected, irrespective of their anatomical structure. Glandular infection on the same side is an early and quite constant occurrence. Even if the disease is correctly diagnosticated at an early stage, complete removal by iridectomy is impossible, as parts of the iris which present a perfectly normal appearance may already be infected and lead to an almost certain recurrence of the disease. Enucleation of the affected eye is only justifiable if the disease affect only one eye, and if the surgeon can satisfy himself that the patient is not suffering at the same time from tuberculosis in other organs inaccessible to successful surgical treatment.

TUBERCULOSIS OF THE SKIN.

All forms of primary tuberculosis of the skin are the result of direct inoculation with tubercle bacilli. Considering the frequency with which abrasions occur in the exposed portion of the skin, and the innumerable sources of infection with the virus of tuberculosis, it is somewhat strange that primary tubercular lesions of the skin are not of more frequent occurrence. Baumgarten believes that this is due to the slow growth of the bacillus and the dense structure of the deeper portions of the skin,—conditions which enable the superficial wound to heal before the tubercle bacilli have penetrated the tissues to a sufficient depth. Considerable confusion exists at the present time in reference to the nomenclature of primary tubercular affections of the skin. We find descriptions of what is called tuberculosis of the skin, *tuberculosis verrucosa cutis*, and lupus, all of which affections have been proved to be tubercular in their origin and manifesting the same clinical tendencies. *It is time that these immaterial and unimportant distinctions should be set aside, and these different affections should be included under one head, as primary tuberculosis of the skin, since all of them present the same histological structure, and all of them are caused by direct inoculation with tubercle bacilli.*

Riehl and Paltauf have described an affection of the skin, under the name of *tuberculosis verrucosa cutis*, in which the bacillus of tuberculosis is constantly found, and which they attributed to local affection, because all of the patients they examined were persons handling animal products. Riehl has also shown the tubercular nature of papillomatous affections occurring upon the hands of pathological anatomists by finding the bacillus in the tissues.

Anatomical and Clinical Proofs of the Tubercular Nature of Lupus.—Lupus vulgaris, and probably the other varieties of this affection of the skin, are nothing more nor less than cases of cutaneous inoculation-tuberculosis. It is well known that lupus occurs most frequently in parts of the body most exposed to injury and infection; that is, in the skin not protected by the hair or clothing. Lupus attacks most frequently the nose, face, eyelids, ears, and hands, localities where abrasions occur most frequently, and parts upon which floating microbes are too liable to become deposited, and where direct inoculation with soiled hands, handkerchiefs, and towels is most likely to occur. I shall quote from a number of reliable authorities at sufficient length to prove that lupus and tuberculosis are identical affections. From a clinical standpoint Hebra brought the different varieties of lupus under one common head. He separated it entirely from syphilis, but otherwise did little to fix its pathological significance. He adopted the classification of Fuchs and the older French and English authors, who taught that it was one of the manifestations of scrofula, and that anatomically it was composed of granulation tissue.

Virchow classified it with the granulomata, but denied its identity with scrofula. Rindfleisch described it as a proliferation of epithelial cells,—as a sort of *phthisis cutanea*. Hueter, who, in his pathological views, was generally far ahead of his time, affirmed that it was a form of *fungous inflammation*, the specific cause of which, when introduced into the organism, produced miliary tuberculosis. Volkmann included it among the affections which anatomically are represented by granulation tissue. Friedländer was the first to take a positive stand in asserting that lupus is a tubercular affection of the skin, and showed its histological identity with other recognized forms of local tuberculosis. He demonstrated the presence of miliary tubercles in it. The absence of caseation in lupus, which was regarded by some authors, among them Baumgarten, as an evidence of its non-tubercular character, has been explained by Schüller as being due to the soil present *in* and *around* the nodules. He also calls attention to the fact that Cohnheim and Thoma have seen caseous foci in lupus, and consequently asserts that the absence of caseation is no proof of the non-tubercular nature of lupus.

Neisser accepts fully and pleads strongly in favor of the tubercular nature of lupus. Rassdnitz collected 209 cases of lupus, and found that in 30 per cent. of all the cases it was associated with other evidences of tuberculosis. He placed, also, great importance on the observations that lupus is prone to develop in the scar left after healing of a localized tuberculosis in lymphatic glands, and that lupus is often observed upon the nose or eyelids in cases of chronic nasal or conjunctival catarrh. In 10 to 15 per cent. of his cases lupus could be traced to hereditary predisposition. Demmé observed miliary tuberculosis in 2 of his cases after scraping lupus. Pontoppindau asserted that, in his experience, in 50 to 75 per cent., patients suffering from lupus manifested additional evidences of tuberculosis. Quinquaud saw in 3 cases of lupus pulmonary tuberculosis appear as a final cause of death. Of 38 cases that came to the personal knowledge of Bessnier, 8 of them suffered from pulmonary phthisis. Of 2 patients treated by Aubert, 1 died of acute pulmonary tuberculosis and the other of tubercular pleuritis after scarification.

Renoward was able to ascertain the existence of pulmonary phthisis in 50 per cent. of his cases of lupus. Block met with tuberculosis in other organs, before or after the development of lupus, in 114 out of 144 cases. Bender examined 374 cases of lupus. In 159 of these an accurate history could not be obtained. In 99 of the latter number symptoms of other antecedent or co-existing tuberculous lesions existed. In 77 of the cases tuberculosis in an etiological or clinical aspect was present. Leloir observed several cases in which, after years, a lupus of the face gave rise to a pseudo-erysipelatous swelling of the face, which disappeared after a time, to be followed by swelling of the submaxillary lymphatic glands, which remained stationary. Soon after the affection of the lymphatic glands had appeared, febrile disturbances, gastric symptoms, and evidences of pulmonary infiltration followed. In all of these cases Leloir believes that the virus of tuberculosis had left the primary location, and had migrated through the lymphatic vessels and glands into the lungs. In 10 out of his 17 cases the tubercular nature of lupus was clinically manifest. Sachs ascertained that, of 105 cases of lupus which he collected, in 86 per cent. the patients had co-existing tuberculosis in other parts of the body, or a hereditary predisposition to tuberculosis could be shown to exist.

Experimental and Bacteriological Evidences of the Tubercular Nature of Lupus.—If the clinical and anatomical proofs which have been advanced to establish the tubercular nature of lupus point unequivocally in that direction, the crucial test is furnished by the inoculation experiments and bacteriological investigations that have been made with the same object in view. Koch, in his paper on the etiology of tuberculosis, states that he produced a pure culture of the bacillus tuberculosis from a case of lupus which resembled in every respect the cultures obtained from recognized tuberculosis, and with the fifteenth generation from this source, one year after the first cultivation, he inoculated 5 guinea-pigs by subcutaneous injection and produced typical tuberculosis in all of them. Doutrelepont found in 7 cases of lupus the bacillus tuberculosis invariably present, in greater or less number, either within the cells or dispersed in small groups between them. He never found them in the interior of giant-cells, but in their immediate vicinity. In a second communication the same author reports 18 additional cases of lupus, in each of which the presence of the bacillus could be demonstrated in the tissues. Demmé detected the bacillus in 6 cases of lupus. Pfeiffer found it in a case of lupus of the [illegible]nctiva. Schuchardt and Krause discovered the bacillus in 3 cases of lupus affecting, respectively, the face, ears, and leg. In examinations made of 11 cases of lupus by Cornil and Leloir, and 4 by Koch, for the especial purpose of showing the identity of lupus and tuberculosis, the bacillus was found in every instance. In the artificial tuberculosis of animals, produced by implantation of lupus-tissue, the specific microbe was shown to exist by Pagenstecher, Pfeiffer, Koch, and Doutrelepont. To prove that lupus and tuberculosis are identical, it became necessary to furnish the necessary experimental proof, and to show the uniform presence of the bacillus of tuberculosis in the lupus-tissue, all of which has been done with almost infallible positive results. The inoculation experiments with lupus-tissue have already been referred to, and from them it can be learned that, with few exceptions, they were followed by positive results; that is to say, implantation of lupus-tissue into subcutaneous tissue or the peritoneal cavity, in animals susceptible to tuberculosis, gave rise to local tuberculosis at the point of implantation and to dissemination of the process in a manner characteristic of tuberculosis in man. A diffuse tuberculosis of the skin and mucous membranes, occurring as a sort of secondary localization in patients suffering from advanced tuberculosis, has been recently described by Pantlen, Bizzozero, Baumgarten, Chiari, Hall, Janisch, Riehl, Vidal, and Finger. As such cases occur in consequence of auto-infection in persons debilitated by the ravages of the primary disease in the lungs, it is not surprising that the skin affection should extend more rapidly than in cases of primary tuberculosis of the skin.

Pathology and Morbid Anatomy.—As every case of tuberculosis of the skin is caused by the entrance of tubercle bacilli from without through some infection-atrium, the primary pathological changes occur at the point of inoculation. As soon as the bacilli reach the vascular layers of the skin, a nodule forms which contains the histological elements described in the section on the Histology of Tubercle. By the formation of new nodules, a more diffuse cellular infiltration of the tissue between them, the lesion tends to spread, and, by confluence of the infiltrated portions, a dense and more or less extensive area of nodular infiltration may be formed. If the continuity of the epidermic layer of the skin has been restored after infection has occurred, and the cell proliferation has been abundant, the swelling may resemble a papillomatous growth, and, on account of the increased vascular supply, an excessive production and exfoliation of epidermis over the infiltrated area occur. These are the cases of inoculation-tuberculosis which have been described as *tuberculosis verrucosa cutis*. The nodules undergo disintegration near the centre, and the epidermis at a corresponding point becomes macerated and detached, leaving at first a minute defect, which secretes a serous fluid.

As soon as the underlying granulation tissue has been exposed to infection from without, infection with pus-microbes occurs, and the destruction of tissue is hastened by the suppuration inflammation which follows, as the granulation cells are rapidly destroyed by the pus-microbes and their ptomaines, and are eliminated as pus-corpuscles. Ulceration now takes the place of the papillomatous growths, and the defect increases in size as rapidly as granulation tissue is produced by the action of the bacillus tuberculosis. New nodules are produced in the immediate vicinity of the ulcer, which are again dissolved by retrograde tissue metamorphosis of its cellular constituents and purulent liquefaction. It is not uncommon to find, at some places, efforts at repair, and even partial cicatrization and epidermization; but the disease pursues its relentless course in other directions, and, after what appears as healthy new tissue, becomes again infected and the process of destruction is repeated. In some forms of tuberculosis of the skin the infection remains superficial, and only the more superficial portions of the skin undergo pathological changes characteristic of tuberculosis; while in other cases the process extends deeper and deeper, until muscles, fascia, and bone are destroyed by the disease, in the manner of its extension from tissue to tissue resembling the clinical behavior of malignant tumors. In this manner the whole nose, eyelids, and the greater portion of the face are frequently destroyed before the patient is relieved from his sufferings by a merciful death. Microscopical examination shows the lesions to consist in the formation of granulation tissue, in which the typical structure and histological elements of tubercle can be readily recognized. Caseation is seldom found, probably on account of the location of the tubercular product so near the surface of the skin, and also because the granulation tissue soon becomes the seat of a secondary infection with microbes which prevent caseation. In most cases a well-marked reticulum is present between the new cells, and these are often grouped in masses around the blood-vessels.

Symptoms and Diagnosis.—Tuberculosis of the skin is most frequently met with in middle-aged persons, but no age is exempt from it, as I have seen it in children 5 years of age and in persons far advanced in years. It attacks most frequently the nose, eyelids, cheeks, ears, and hands, but it may also develop upon the different parts of the trunk. The disease commences in the form of a small, red, vascular nodule; is not painful nor tender on pressure. In the vicinity of this nodule new foci spring up, and by confluence may form a swelling of considerable size. To the touch these nodules impart rather a sensation of elasticity than hardness, and if the swelling is large in size an obscure sense of fluctuation may be felt. Before ulceration takes place the surface of the nodules is covered by a thickened epidermis, which can be scraped off in white scales. If no ulceration take place (*lupus non-exedens*), the nodules may remain stationary in size for an indefinite period of time or undergo a spontaneous cure by cicatrization, during which the epithelioid cells are converted into connective tissue. Ulceration begins over the centre of the nodule, at a point where the nutrition of the tissues is most impaired by pressure, and extends from here toward the margins of the nodule, attacking the new nodules almost as fast as they are formed (*lupus exedens*). Cicatrization and ulceration are often seen side by side. Ulceration is hastened by the secondary infection with pus-microbes, which invade the granulation tissue in the margins of the ulcer, occupying the tubercular zone. Repair by cicatrization and epidermization is more likely to occur if the infection remains superficial, but is usually entirely absent as soon as the tubercular process has extended beyond the limits of the skin. The differential diagnosis as to tuberculosis of the skin, tertiary syphilis, and epithelioma is generally very difficult, and sometimes almost impossible. There is very little difference between the histological structure of a tubercle-nodule and a gumma, and the most experienced microscopist is liable to make a mistake if called upon to make a diagnosis exclusively by the use of the microscope.

The history of the case is of the greatest importance in making a differential diagnosis between tuberculosis and syphilis. If the patient is positive that he never contracted syphilis, it is still possible that the lesion may be syphilitic, as the disease may have been inherited; if he give a history of primary and secondary syphilis, the affection may still be tubercular; but a straight history of tuberculosis or syphilis will go far in determining the nature of the local affection. If any doubt remain, this can be cleared up by the use of the microscope in the course of five weeks, either by the effect produced by anti-syphilitic treatment or the result of inoculation experiments made by implantation of fragments from the inflammatory product into the subcutaneous tissue in guinea-pigs. The microscopic examination of fragments of tissue removed for this purpose must have in view the detection of the bacillus of tuberculosis, which is constantly present in tubercular tissue. The specimen must be prepared by double staining according to Ehrlich's method, and if the affection is tubercular, the bacillus can be found by making a patient search for it; if it is syphilitic, it will, of course, be absent. The bacilli, however, may be so few that even a careful search of stained specimens may result negatively, and in such a case a positive diagnosis can often be made by observing the effects of a thorough anti-syphilitic treatment. For an adult, $\frac{1}{30}$ grain of sublimate with 15 grains of potassic iodide, dissolved in distilled water, is given four times a day,—after each meal and at bed-time. If the lesion is syphilitic, a decided improvement will be observed in the course of two or three weeks; if tubercular, this treatment will make no decided impression on the local lesion. The most reliable diagnostic test in differentiating between tuberculosis of the skin and a syphilitic lesion consists in removing, under antiseptic precautions, a fragment of granulation tissue the size of a small pea, and implanting the same into the subcutaneous tissue of a guinea-pig.

Tavel has been studying, in a systematic manner, the diagnostic value of implantations of tubercular material in animals, mainly guinea-pigs. He found that fragments of granulation tissue, taken from a tubercular product and implanted into the subcutaneous connective tissue in the inguinal region in guinea-pigs, invariably produces in this animal local, and later general, miliary tuberculosis, and death in from five to six weeks. The course of the disease thus artificially produced is typical; at the point of inoculation a hard nodule appears first, the result of traumatic response on the part of the tissues around the graft. Next, a lymphatic gland becomes enlarged in the immediate vicinity of the inoculation and in the direction of the lymphatic stream. Often all of the inguinal glands are infected successively. At a later stage the axillary glands become affected At the necropsy it was always observed that, of the internal organs, the spleen becomes affected first, then the liver and lungs, but before death is produced almost every organ is the seat of miliary nodules. When the differential diagnosis between tuberculosis and syphilis cannot be made from a clinical study of the case or by the use of the microscope, inoculation experiments will always furnish the desired information in from three to six weeks. If the lesion is tubercular, the infected guinea-pig contracts the disease, and dies in from five to six weeks; if it is syphilitic, the implantation will prove harmless and the animal remains well. The differential diagnosis between tuberculosis of the skin and epithelioma must be based on the primary location of the pathological product and the character of the infiltration. Tuberculosis commences in the vascular portion of the skin; hence, the primary nodule is sub-epidermal; while epithelioma starts in the non-vascular epidermis and infiltrates the deeper layers of the skin later. The tubercular nodule is not hard, but somewhat elastic, to the touch. The carcinomatous infiltration feels almost as hard as cartilage, and forms a part of the epithelial layer of the skin from the beginning. A tuberculous ulcer of the skin is covered with flabby granulations, and its margins, although infiltrated, do not feel as firm as the borders of an ulcerating epithelioma. Under the microscope the tubercle-nodule shows granulation cells in the meshes of a delicate reticulum, while in a section of an epithelioma a well-marked alveolated reticulum can be seen, the meshes of which are occupied by embryonal epithelial cells arranged in concentric layers. Another microscopic criterion is the absence of blood-vessels in tubercle-nodules, while carcinoma is a vascular structure.

Prognosis.—Primary local tuberculosis of the skin may lead to glandular infection, and, after the last lymphatic filter has been passed, to general miliary tuberculosis. The tubercular product in exceptional cases becomes the starting-point of carcinoma. The local extension of the tubercular process is subject to many variations. In some instances the process commences during early life, and remains stationary for twenty or more years, when it suddenly commences to extend very rapidly, destroying all of the tissues which come in its way, irrespective of their anatomical structure. Tuberculosis of the face, manifesting such a tendency to rapid extension, may in a few months destroy nearly all of the soft tissues and a considerable portion of the superficial bones, so that the head looks more like a skull than the head of a living being. In other instances the ulceration keeps extending, while at other points the healing process is progressing with equal speed. In such cases the massive scars are often productive of the most hideous deformities. Recurrence of the disease in the scar-tissue is of common occurrence. The prognosis, as far as life is concerned, is favorable so long as the disease remains local and does not progress rapidly; while life is threatened as soon as regional infection through the lymphatic glands takes place, or when ulceration extends rapidly without any tendency to repair by cicatrization and epidermization. Tuberculosis of the skin without ulceration is a more benign form of the disease than when ulceration has occurred, as in the latter case the destructive process is hastened by secondary infection with pus-microbes.

Treatment.—About the only medicine that deserves any confidence in the treatment of tuberculosis of the skin is *arsenic*. This drug can be given in the form of Fowler's solution, in doses of from 3 to 10 drops after each meal, well diluted with water. It is best to commence with the smallest dose and add 1 drop every week until the physiological effect is produced, when the use of the medicine is not suspended, but the dose is diminished. To be of any use, the medicine has to be continued for weeks and months. If the patient is anæmic, it is combined with the tincture of chloride of iron, and, if the patient's appetite is poor, with one or more of the bitter tonics. If the patient is emaciated, pure codliver-oil can be given with good results an hour and a half after meals, in doses which will be tolerated by the stomach. If digestion is impaired this drug should be withheld. A well-selected, nutritious diet is indicated in all such cases, with plenty of out-door exercise. Salt-water baths invigorate the peripheral circulation, and consequently favor the limitation of the disease and the process of repair. The surgical treatment of tuberculosis of the skin is to be conducted upon the same principles as operation for the removal of malignant tumors. The use of caustics often does more harm than good. *The great object of the local treatment is to remove every particle of the infected tissues, for if this is not done a recurrence is almost sure to take place.* If the patient object to a radical operation, and the tubercular process has gone on to ulceration, all irritating applications should be avoided and the ulcer protected by a piece of lint spread with empl. hydrargyri or unguent. hydrargyri oxyd. albi. Balsam of Peru can also be used with benefit as a local application. If a radical operation is decided upon, this should be done preferably by excision. Excision should be practiced exclusively in cases where the extent of the disease is limited. The incision should be made some distance from the visible margins of the infiltration, in order to include tissues which, although presenting macroscopically a healthy appearance, may already be infected with bacilli, conveyed there by migrating leucocytes. The greatest care must be exercised in removing the deeper portions of the inflammatory product, as this may send down projections at different points which it is necessary to remove with the principal mass.

Thiersch's method of restoring the excised skin places the surgeon in a position where he can excise an extensive area of tegument, and yet obtain primary healing of the wound and perfect restoration of the skin under a single dressing. I have, on several occasions, removed tubercular foci from the face and temporal region the size of the palm of the hand, and, by covering the defect at once with large skin-grafts, saw the whole healing process completed in two weeks, with almost perfect restoration of the lost tissues. In cases where the disease is too extensive for excision, removal of the infected granulations is attempted by the vigorous use of Volkmann's sharp spoon. Skin-grafting can be done after curetting in the same manner as after excision, but the knife always leaves a better surface for skin-grafting than the sharp spoon. If, after either operation, the result is not perfect, and the tubercular process returns at one or more points, the granulations are again removed with the sharp spoon and the defect covered with skin-grafts. Tuberculosis without ulceration demands treatment by excision, while in the case of ulcerating nodules the ch [illegible] ife and sharp spoon, and to the first preference should be given in all cases where excision can be done with a fair prospect of removing all of the infected tissues. The constitutional treatment should be continued for several months after the local lesion has apparently healed, as the disease is very liable to recur at the site of operation. The site of operation should be carefully protected against injury a long time after the process of repair has been completed, in order to guard against a return of the disease, from local irritation preparing the soil for the pathogenic action of latent bacilli which may remain incorporated in the scar-tissue.

CHAPTER XIX.

TUBERCULOSIS OF LYMPHATIC GLANDS AND PERITONEUM.

TUBERCULOSIS OF LYMPHATIC GLANDS.

THAT most cases of chronic inflammation of the lymphatic glands are in their origin, course, and final termination instances of local tuberculosis, has been satisfactorily shown by clinical experience, microscopic examination, inoculation, and cultivation experiments.

Manner of Infection and Dissemination of the Bacillus of Tuberculosis.—The tubercle bacilli enter the lymphatic circulation through some abrasion or pathological defect of the skin or mucous surface; any loss of continuity of surface may furnish the necessary *portio invasionis* for the entrance of the microbes from without. In tubercular affections of the skin the point of inoculation becomes the centre of the primary nodule, because the bacilli are present in sufficient quantity and virulence to produce the necessary irritation; but in tuberculosis of the lymphatic glands the microbes enter the lymphatic channels usually before they have caused any visible lesions at the point of entrance.

Volkmann found tubercle bacilli in the skin of an eczematous forearm, and it is probable that many cases of tuberculosis of the cervical glands in children are caused by the entrance of tubercle bacilli through an eczematous patch on the face, ear, or scalp. In perhaps 95 out of every 100 cases of tuberculosis of the lymphatic glands the disease attacks the glands of the neck,—as the scalp, face, and mouth are parts of the body most frequently the seat of slight injuries and superficial lesions, and also most exposed to tubercular infection. The lymphatic glands act as filters for the microbes which enter the body through the lymphatic channels. The pathological conditions which are produced in the interior of a lymphatic gland by the presence of pathogenic micro-organisms are well calculated, for the time being at least, to limit the extension of the infection. The lymphadenitis which is produced blocks the lymph-spaces with the products of a specific inflammation, which, temporarily at least, mechanically obstructs the way for the microbes toward the general circulation. Primary infection of a lymphatic gland by the bacillus of tuberculosis in many instances attacks different portions of the gland from the very beginning, as a [illegible] nt centres of tissue proliferation are established around each microbe, or around each colony of microbes arrested on their way through the gland. These separate nodules soon become confluent and form a mass of considerable size, which soon implicates the entire parenchyma of the gland. Local dissemination of the bacillus of tuberculosis in the interior of the gland is accomplished by the assistance of the lymph-stream, as long as the microbes remain free, and through the medium of wandering cells as they have become attached to or have entered the protoplasm of the lymphoid corpuscles and leucocytes.

Regional infection is not limited to the lymphatic glands, on the proximal side of the primary focus, as during the course of the disease we often observe that lymph-glands become involved which are not in the direct course of the lymph-stream. As the bacillus of tuberculosis is non-motile, we can only explain its transportation in a direction opposite the lymph-current by its conveyance in such a direction by migrating amœboid cells. As the lymph-stream is impeded or perhaps completely arrested by the inflammatory product which has accumulated in the lymph-spaces, migration of leucocytes in an opposite direction is easily explained. The usual course of infection along the lymphatic channels is, however, in the direction of the lymph-current. The course of the disease is almost characteristic. A lymphatic gland in the submaxillary or parotid region becomes enlarged, and from this centre the infection invades successively gland after gland, until the whole chain of lymphatics from the angle of the lower jaw to the clavicle has become involved. Another interesting feature is observed in reference to the regional diffusion of the tubercular process, as the course of infection usually corresponds to the location of the gland first affected. If the infection has involved primarily one of the deep glands of the neck, the glands subsequently invaded belong to the deep lymphatics which follow the larger blood-vessels of the neck. If, on the other hand, the primary depot is located in one of the superficial glands, the glands, which are being irrigated by the lymph that flows through and from the gland, become the seat of successive infection, showing again that regional infection usually takes place in the direction of the lymph-current. In extensive tuberculosis of the glands of the neck, the superficial and deep glands are affected at the same time, the infection from one set of vessels to the other being accomplished through the medium of communicating branches. As long as the infection has not extended along the entire length of the chain of lymphatic glands, the patient is protected against miliary tuberculosis; but as soon as the virus has passed all of the lymphatic filters it enters the general circulation, and diffuse miliary tuberculosis follows as an inevitable result.

Pathological Histology and Morbid Anatomy.—As soon as a sufficient number of bacilli has entered the parenchyma of a lymphatic gland, a karyokinetic process is initiated which involves the parenchyma-cells, the cells of the reticulum, and the endothelial cells. The proliferating tissue-cells produce epitheloid and giant cells, while the lymphoid elements are either the normal lymphoid corpuscles, which have remained unaffected by the inflammatory process, or leucocytes. As the number of bacilli present is not great, the process is a very slow one, and the inflammatory product undergoes very gradually the characteristic degenerative changes. The entrance of new bacilli from the infection-atrium is prevented by the obstruction in the lymph-spaces, caused by the accumulation within them of the products of inflammation, which arrests the lymphatic circulation in the afferent vessels of the gland, through which primarily the bacilli entered. The bacilli found in the tubercular gland are, therefore, derived from the multiplication of the bacilli which originally entered the gland from the primary infection-atrium. The cells that first undergo coagulation necrosis are those in the centre of each nodule, for reasons which have been previously mentioned. As the products of coagulation necrosis do not furnish the necessary nutritive material for the growth of the bacillus, the microbes gradually disappear in the centre of the nodule, while they can still be found within and between the cells in the surrounding granulation tissue. Cell necrosis is followed by caseation, and by this time nearly all of the bacilli have disappeared, but inoculation experiments with cheesy material have shown that spores remain in an active condition, and capable of reproducing the disease in animals. The numerous nodules which appear, often almost simultaneously, in the interior of the same gland become confluent, and in the course of time the entire parenchyma of the gland is destroyed, while the intact capsule of the organ still furnishes a wall of protection against infection for the surrounding tissue. A single tubercular gland is seldom larger than a walnut, and the large masses found in the neck and other regions are composed of several glands so closely packed together as to give the appearance of a single gland. When the capsule becomes infected, the same processes are initiated here as in the parenchyma of the gland; the connective tissue is transformed into granulation tissue, which undergoes coagulation necrosis and caseation in the same manner as the fixed tissue-cells of the parenchyma; and, finally, after perforation of the capsule has taken place, the inflammation extends to the paraglandular tissues, resulting in tubercular periadenitis. The cheesy material may dry and shrink and become inclosed by a capsule of dense connective tissue, resulting in calcification; or it undergoes liquefaction. If secondary infection with pus-microbes take place, a not infrequent occurrence in tuberculosis of the glands of the neck, an acute suppurative inflammation takes the place of the chronic process, and almost without exception results in a rapidly-spreading suppurative periadenitis. The connective tissue surrounding the gland becomes swollen and œdematous and large abscesses form, which, on being incised, give exit to pus which resembles the pus of an ordinary phlegmonous inflammation. The suppurative inflammation results in extensive detachment of the cheesy glands, which at this time can be readily enucleated by the finger. If, however, the abscess is simply incised, and the radical operation postponed for weeks or months, the removal of such glands is an exceedingly difficult task, as the capsule of the gland will then be found intimately adherent throughout the surrounding tissues.

Symptoms and Diagnosis.—Tuberculosis of the lymphatic glands occurs most frequently in persons between 15 and 30 years of age. The regions most frequently affected are the cervical, parotid, submaxillary, axillary, and inguinal. Tuberculosis of the parotid, submaxillary, and cervical lymphatic glands is often preceded by eczema of the scalp, ears, or face, or by a catarrhal or tubercular inflammation of the mucous membrane lining the nose and pharynx. It is possible that in many of these cases the catarrhal inflammation creates the necessary infection-atrium for the entrance of the bacilli into the lymphatic channels; or, what is more probable, that which has been regarded as a catarrhal inflammation is, in reality, a mild tubercular inflammation that may disappear after infection of the lymphatic glands has occurred. In the region of the neck, the first glands affected are usually the submaxillary, or the glands just behind, in front, or below the external meatus. Progressive infection is the most characteristic clinical feature of tuberculosis of the lymphatic glands. Regional infection, as has been stated, usually takes place by the extension of the disease from gland to gland, until the whole chain in a region has become affected. In a case far advanced, for instance, the glands first affected may be as large as a walnut; their size then gradually diminishes, so that those last infected may not be larger than a split pea. The degenerative changes are also most marked in the glands first affected; so that, while the primary foci show well-marked evidences of caseation, and caseation with liquefaction, the glands last infected still present a normal pinkish color. The number of glands affected in one region varies from one to twenty or more. If many glands are affected, the hyperplastic inflammation in their periphery usually results in their becoming matted together into a dense nodular mass. With the exception of the neck, it is seldom that more than one anatomical region is affected. In the cervical region it is not uncommon to find the glands on both sides affected at the same time. The infected glands increase gradually in size; they are painless and not tender on pressure. At first they are movable, and appear loosely attached to the surrounding tissues. With the appearance of periadenitis the swelling rapidly increases in size, and the gland becomes fixed and immovable. Liquefaction of the cheesy material is announced by softening and perceptible fluctuation. Secondary infection with pyogenic microbes is followed by phlegmonous inflammation in the capsules and in the connective tissue surrounding the affected glands. The course of the disease, so far as time is concerned, is extremely variable. The extension of the infection and the growth of the swellings may become arrested for months or years, when the disease may take a new start and pursue its typical course. I recollect the case of a woman, 45 years of age, who had an enlarged gland the size of a hazel-nut in the upper cervical region, which remained stationary for twenty years, when the swelling rapidly increased in size; new glands became infected, and, when the glands were removed by operation, it was seen that the first gland was composed of a thickened capsule, distended to its utmost by inspissated cheesy material. The capsule showed evidences of recent tubercular inflammation, and small foci of caseation were detected in the glands that had recently become infected. When a true suppuration takes place in a tubercular lymphatic gland, it does so in consequence of a secondary infection with pyogenic micro-organisms. A spontaneous and permanent cure is not infrequently effected by the substitution of an acute suppurative process in place of the primary specific chronic inflammation, which destroys the entire soil of the bacillus tuberculosis and, at the same time, effects complete elimination of the bacilli through the discharges of the abscess. While tuberculosis of the lymphatic glands often stands in a direct causative relationship to and precedes general, diffuse, and pulmonary tuberculosis, it is seldom observed as a secondary affection in the course of pulmonary tuberculosis. I have observed one case of tuberculosis of the lungs with secondary infection of the lymphatic glands. The patient was a woman, 50 years of age, who had suffered for two years from well-marked typical tuberculosis of the lungs, when the glands on both sides of the neck became infected, and continued to increase in number and in size until she died, six months later. Fränkel reports an interesting case in which lymphatic and pulmonary tuberculosis developed almost simultaneously. The patient was a woman, 51 years of age, who had given birth to two children, their father being the subject of advanced tuberculosis, and both of whom died of tuberculosis. She had been in perfect health until her 49th year, when she was attacked simultaneously with pulmonary and glandular tuberculosis, from the continued effects of which she died in a few months. In exceptional cases glandular tuberculosis pursues an acute course. Delafield reports an exceedingly interesting case of this kind. The disease commenced with enlargement of one of the cervical glands near the angle of the lower jaw, with a temperature of 40° C. (104° F.), and rapid extension to the proximal glands as far as the clavicle. Symptoms of pulmonary complication were not present. Rapid emaciation and marked anæmia supervened, followed after six weeks by swelling of axillary and inguinal glands. Ophthalmic examination revealed the same conditions of retina and papilla as in leucæmiá or Bright's disease. A few days after the beginning of the disease profuse diarrhœa and reduction to nearly normal temperature occurred. The diagnosis was between malignant lymphoma and tubercular adenitis. During the further course of the disease bronchial breathing in both lungs appeared. Heart, liver, and spleen appeared to be normal. Urine normal, but increase of temperature and respirations took place during this time. Death occurred in less than five months. At the autopsy the lungs were found congested and œdematous, with red hepatization of the lower lobes and a few miliary tubercles. The spleen contained many miliary tubercles the size of the head of a pin, and most of them in a state of cheesy degeneration. The mesenteric glands were much enlarged, and a few of them in a condition of cheesy degeneration and calcification. In the cheesy matter bacilli were found. All the cervical glands were affected with softening and cheesy degeneration in the centre. The calcification of mesenteric glands pointed to an earlier affection. The disease remained latent and recurred in the same glands, and, later, extended to the cervical glands. This case resembles the cases described by Hilton-Fagge and Pye-Smith.

In reference to the dissemination in cases of acute miliary tuberculosis, Weigert has pointed out that in some cases the bacilli are conveyed through the lymphatic system successively until they reach the general circulation, while in others, and by far the greater number, generalization of the tuberculous process takes place more directly by the entrance of tubercular products through a vein,—an occurrence which is followed at once by rapid and extensive diffusion by embolic processes; when the bacilli have reached the systemic circulation, the intensity of symptoms and subsequent course of the disease depend on the number of bacilli which the blood contains. As regards the frequency of secondary infection of the lungs in cases of glandular tuberculosis, Fränkel found it present in only 18 out of 148 cases. In making a differential diagnosis it becomes necessary to distinguish tubercular adenitis from simple adenitis, suppurative adenitis, syphilitic adenitis, carcinoma, lymphoma, lympho-sarcoma, and pseudo-leucæmia.

Simple adenitis is the result of the entrance into the lymphatic circulation of noxæ that neither produce suppuration nor the formation of new tissue. A number of glands corresponding to the direction of the lymph-current from the infection-atrium, through which the irritant gained entrance, enlarge, but the inflammatory swelling subsides shortly after the cessation of the primary cause, with perfect restoration of the structure and function of the affected glands. Suppurative adenitis is an acute affection which terminates in the formation of pus in a few days. Syphilitic adenitis developing in the course of a primary syphilitic sore only attacks the glands contaminated with lymph coming from the infected area. The adenitis which accompanies secondary and tertiary syphilis is not limited to a single region; nearly all of the external lymphatic glands are more or less enlarged, but especially those in the occipital and cubital regions. Carcinoma never occurs as a primary lesion in the lymphatic glands, and when regional infection has occurred it is not difficult to locate the primary tumor. Lymphoma is a benign tumor of the lymphatic glands, and as such is always met with as a single tumor. Lympho-sarcoma represents the primary malignant tumor of the lymphatic glands, and gives rise to regional and general infection, the infection in these respects resembling the clinical tendencies of tubercular adenitis. Lympho-sarcoma, however, is a tumor, not an inflammatory swelling, and, consequently, the tissues of which it is composed do not undergo degeneration and necrosis at such an early stage, and the rapid tissue increase leads to the formation of large tumors, while tubercular glands the size of an almond contain cheesy material. The unlimited growth which characterizes sarcoma is checked in the tubercular glands by necrosis of the cells which compose the swelling. In pseudo-leucæmia the fixed tissue-cells of the parenchyma of the glands proliferate by being acted upon by a microbe as yet unknown; but this microbe, unlike the bacillus of tuberculosis, is diffused more extensively through the lymphatic system, involving one region after another until, after the disease has been once well developed, almost every lymphatic gland in the body has become infected. The supposed microbe of pseudo-leucæmia possesses the property of producing new tissue by its action upon the fixed cells, but the new product does not undergo caseation. As the last and infallible diagnostic measures, must be mentioned the search for the bacillus of tuberculosis by the use of the microscope and inoculation experiments.

Prognosis.—A tubercular lymphatic gland is always a source of danger. Even if the disease becomes latent, a recurrence may take place at any time, and lead to rapid regional and general infection, or general infection may take place directly from an old cheesy focus by the entrance of bacilli or their spores into a vein. The prognosis is very grave if the patient is anæmic, and the glands on both sides of the neck are affected at the same time. Fränkel estimates the average duration of the disease from three to four years. In the cases which he collected the shortest time was two months and the longest thirty years. Sooner or later, pulmonary or diffuse general tuberculosis is almost sure to take place. A spontaneous cure is possible if secondary infection occur in cases where only a few of the glands have become infected, and suppuration results in the elimination of all the infected tissue. Suppuration only hastens a fatal termination if many glands are affected.

Treatment.—As primary lymphatic tuberculosis, in most instances, signifies the entrance of bacilli through a loss of continuity of the skin or a mucous membrane, or through the socket of a carious tooth, localization occurring in one of the nearest glands to the *portio invasionis*, it must be regarded primarily as a local process amenable to timely surgical treatment. The capsule of the lymphatic glands constitutes a very efficient barrier against infection of the paraglandular tissue for a long time, and perforation of the capsule can only take place after the disease has made considerable progress, and has been followed by extensive caseation and especially by suppuration. *Early operative interference is as necessary in the treatment of tubercular adenitis as in the treatment of malignant tumors, and holds out more encouragement, so far as a permanent cure is concerned.* By a thorough removal of the primary foci of infection, successive infection of proximal glands and general miliary tuberculosis are prevented almost to a certainty if the operation is performed before the disease has extended beyond the capsule of the glands. If the operation is done at such a favorable time it is not attended by any great difficulties, as the glands can be readily enucleated, and, as suppuration has not taken place, the wound usually heals by primary intention. If, however, the tubercular inflammation has involved many glands, and has extended to the connective tissue surrounding them, the operation becomes one of the most formidable in surgery, on account of the close proximity of important vessels that are often imbedded in the mass. Under such circumstances complete removal is frequently impossible and early local recidivation is inevitable, owing to imperfect removal of the primary microbic cause. Traumatic dissemination is very likely to follow all imperfect operations in which portions of glands or infected capsules are left behind, as the operation wounds are inoculated with bacilli liberated during the operation. I have seen in a number of such cases, as early as a week after the operation, the entire surface of the wound covered by a thick layer of granulation tissue, which showed all the histological evidences and possessed all the bacteriological properties of tubercular tissue. As a testimony in favor of the operative treatment of tubercular adenitis, I will quote from the paper of Schuell, who collected 56 cases of tuberculosis of the cervical glands that were treated by extirpation in the clinic at Bonn. In 37 of these cases he was able to learn the ultimate result. In 57 per cent. the operation was followed by complete recovery, in 27 per cent. the disease returned at the site of operation, and in 4 cases death resulted from pulmonary tuberculosis. The largest number of cases were patients between 10 and 20 years of age.

Fränkel reports 128 cases operated upon by Billroth, some of the operations being quite serious; in 16 cases the internal jugular vein had to be tied. In 91 of the operations the wound healed by primary union, and in 25 the healing was retarded by suppuration. Erysipelas complicated the result five times. In one of these cases a large part of the tubercular mass was left, and it was noticed that the erysipelas had no effect on the tubercular process. Only in 49 of the cases operated on could the final result be obtained. Taking three and a half years as the time when the patient could be considered exempt from a recurrence of the disease, it was ascertained that in 24 per cent. no relapse followed the operation, a local relapse was observed in 14 per cent., and re-appearance of the disease distant from the seat of operation in 4 per cent. The results of operation for tuberculosis of the lymphatic glands have shown the necessity of early operating, as delay renders the operation more difficult, on account of the progressive regional dissemination of the disease and the occurrence of pathological changes within and around the affected glands, which render their complete removal more difficult; while at the same time the danger of general infection increases with the local extension of the disease. If the glands have suppurated, or if the capsule has become perforated and tubercular periadenitis or suppurative periadenitis has taken place, and many glands are simultaneously affected, it may not be advisable to resort to excision, as when extensive connective-tissue infiltration is present it would be almost impossible to remove all of the infected tissues.

In such cases free incisions should be made, and the tubercular product be removed with a Volkmann spoon. The proximal glands which have not undergone such extensive secondary pathological changes can be excised. The scraped surface is freely iodoformized and the wounds are sutured and drained. In removing the glands of the neck it is always important to expose the infected area by a large incision. *The operator should not only feel, but see, every gland he removes.* Accidents are more liable to happen by removing the glands through a small than a large incision. As in cases of secondary carcinoma of the lymphatic glands the extent of the disease is only ascertained after incision, so in glandular tuberculosis the extent of the area of infection can only be ascertained after the external incision is made. Whole chains of small glands which could not be felt through the skin are then exposed. In tuberculosis of the glands of the neck the region between the mastoid process and the angle of the lower jaw is almost always the primary seat of infection. From here either the chain of glands behind the sterno-cleido-mastoid muscle or the deep glands which follow the sheath of the large vessels of the neck are affected, or the superficial and deep lymphatics are affected simultaneously. It has been my custom to expose the glands occupying the upper region of the neck by a transverse incision, extending from the tip of the mastoid process of the temporal bone to the lower angle of the jaw, and from there along the lower border of the bone, as far as the disease extends in the submaxillary region. This incision is joined by another, extending from the angle of the lower jaw either along the anterior border of the sterno-cleido-mastoid muscle as far as its sternal insertion, if the deep glands are to be removed, or, if the posterior superficial set of glands are affected, it is carried in a downward and backward direction, following the chain of enlarged glands. If the latter incision is selected, the external jugular vein is divided between two ligatures. The platysma myoides muscle is divided throughout the whole length of the incision before an attempt is made to remove any of the glands. *The surgeon should aim to remove, as nearly as he can, all of the infected glands in one disconnected string.* In many cases one or two tubercular glands will be found imbedded in the lower portion of the parotid gland, and very frequently also in the submaxillary salivary gland. If the tubercular glands, with their capsules, can be enucleated, this should be done; but if this is impossible, it is better to remove the lower portion of the parotid with them in preference to leaving any infected tissue behind. Under the same circumstances I prefer to extirpate the submaxillary gland *in toto.* If the deep glands of the neck must be removed, it is absolutely necessary to divide the sterno-cleido-mastoid muscle near its centre, and then reflect both ends nearly as far as the origin and insertion of the muscle, which freely exposes not only the affected glands, but also the important structures of the neck, which it is important to avoid in the dissection. The dissection must always be made with the greatest care, and in the vicinity of the large vessels every structure must be identified before it is separated. The finger and blunt-pointed, curved scissors are the most important instruments in making the deep dissection. The internal jugular vein should be seen before any of the deep glands are removed, for if this structure is seen it can be carefully followed the whole length of the neck without wounding it unintentionally. If the internal jugular vein is imbedded among the enlarged glands, and cannot be isolated without great danger of injuring it, it is better to resect it between two ligatures than to run the risk of wounding it accidentally. The chain of enlarged glands is followed as far as possible, as it is much better to remove a few healthy lymphatic glands than to leave minute, almost invisible foci of the disease. After all of the infected glands have been removed the continuity of the divided muscle is restored by suturing. At least six catgut sutures are necessary to join the thick ends accurately. I have usually succeeded in removing all the glands after division of this muscle without dividing the spinal accessory nerve, but, should this be necessary, the divided ends are joined by suturing before the muscle is united. Drainage in the submaxillary region and at the most dependent point of the wound in the neck must always be established. The platysma muscle should be united with buried sutures before the skin is sutured. Wounds of the neck, on account of the irregular outlines of the neck, shoulder, and chest, require a very copious antiseptic dressing to effectually exclude the entrance of pathogenic micro-organisms after the operation. The dressing should be kept in place by a few turns of the plaster-of-Paris bandage, which also keeps the head in proper position during the time required in the healing of the large wound. The sutured muscle must be kept in a relaxed position until firm union has taken place between the sutured ends, which usually requires from two to three weeks. On the second or third day the dressing is changed, the drains are removed, and, if the wound has remained aseptic, the second dressing can be allowed to remain for ten days or two weeks, when it is changed, and the superficial stitches are removed. If all of the diseased tissues have been removed, and the wound has remained aseptic, the healing process will be found nearly completed at this time.

Local recurrence of the disease should only stimulate the surgeon to continue the active warfare, and glands are removed as soon as they can be felt. I have repeatedly performed, on the same patients, three and four operations in as many years, and had the satisfaction of finally eradicating the disease completely. Parenchymatous injections of carbolic acid, so strongly recommended by Hueter in the treatment of tubercular glands, have little or no effect in either arresting further development of the disease in the affected glands or in preventing further regional infection. I have seen, in cases treated by this method, glands finally destroyed by suppuration caused by the punctures; but the bacilli remained in the cicatricial tissue, as was evident by the œdematous, congested scar, and from here additional glands became infected.

Genzmer advised ignipuncture in the treatment of tubercular glands, and claims for this method excellent results. This treatment is applicable only in cases where a few of the more superficial glands are affected, and where patients positively refuse to submit to a more radical procedure. It is absolutely contra-indicated when many glands are affected, as in cases where the glands are affected they have undergone extensive secondary pathological changes. The general treatment of tuberculosis of the lymphatic glands is the same as in the other forms of local tuberculosis. I have seen the best effects from the administration of arsenic and iron, followed or alternated by codliver-oil. All external applications to bring about resolution are worse than useless.

TUBERCULOSIS OF PERITONEUM.

Tubercular peritonitis occurs as one of the lesions of acute general tuberculosis, with chronic pulmonary phthisis, with tubercular inflammation of the genito-urinary tract, and as a local inflammation. As a surgical lesion only the local form will be considered here.

Bacteriological Remarks.—The susceptibility of the peritoneum to tubercular infection has been well established by numerous inoculation experiments. The peritoneum can, under favorable conditions, dispose of a large dose of a pure culture of pus-microbes, but the implantation of a minute fragment of tubercular tissue in animals susceptible to tuberculosis is almost certain to be followed by genuine local and general tuberculosis. For the surgeon, only those forms of peritoneal tuberculosis have interest which are either caused by an extension of an adjacent tubercular process to the peritoneum or from primary localization of the bacillus within or upon this membrane. The prevalence of the affection in the female sex among the cases which have been reported points to the Fallopian tubes as a frequent primary seat of infection, with secondary invasion of the peritoneum from this source. Although the genital organs in the male are more frequently the seat of tuberculosis than in the female, so far only 2 cases of peritoneal tuberculosis in males have been reported,—1 by Kümmel and the other by Lindfors. Tuberculosis of the peritoneum, by extension from a tuberculous focus in the genital organ, can only mean an infection by contact, the bacillus of tuberculosis transferred from the primary seat of infection, and localization by implantation upon the peritoneal surface. Implantation experiments in animals furnish a good illustration of the manner in which the process becomes diffuse. At the point of implantation a granulation mass forms around the graft, and from here innumerable tubercle-nodules take their starting-point, forming everywhere new centres of infection. The movements of the abdominal walls during respiration and the peristaltic action of the intestines are potent factors concerned in the local dissemination of the tubercular infection. Anatomically, the peritoneum is so closely allied to the lymphatic glands that we have every reason to believe that primary tuberculosis can occur in this structure as well as in the lymphatic glands. In primary tuberculosis of the peritoneum infection takes place in the same manner as in intact joints, by floating bacilli becoming arrested in the capillary vessels of the membrane, where the primary nodule forms, from which, again, as from a graft, local dissemination takes place. These cases are, in the true sense of the word, not cases of primary tuberculosis, as the peritoneal affection is only a local expression of an antecedent infection. As the peritoneum is endowed with absorptive capacities of a high degree, and is in direct communication with the lymphatic system, we would naturally expect that tuberculosis of this structure would lead to early general dissemination. But in peritoneal tuberculosis we observe the same tendency to limitation of the infective process as in joints, by the formation of an impenetrable wall of connective tissue, which imparts so often to this form of peritonitis its circumscribed character.

Clinical Studies.—Kümmel looks upon peritoneal tuberculosis as a purely local affection, amenable to surgical treatment in the same sense and to the same extent as a tuberculosis of joints. That some of these cases can be permanently cured by local treatment is well shown by a case treated by Sir Spencer Wells twenty-six years ago by abdominal section, the patient having remained up to this time in perfect health. In a recent paper on this subject Fehling reports 4 cases of his own, and gives an account of all the operations which had been done up to that time,—21 in number. Of this number 15 recovered, and the patients are known to have been well from one year to twenty-three years, and in a number of cases their condition was learned four to five years after the operation. Six of the patients died,—2 of sepsis, 1 of pyæmia several months after the operation, and 3 from the continuance of the disease for which the operation was performed. In 5 of the cases ascites attended the tuberculosis; in 3 the swelling was not due to effusion, but to adhesions between intestinal loops that were covered with miliary tubercles.

Of 54 cases of laparotomy for peritoneal tuberculosis, collected by Trzebicky, 4 died from the immediate consequences of the operation, while in a fifth death occurred after the operation from acute miliary tuberculosis, though the fluid had not re-accumulated. One case died in four months from general tuberculosis without the peritonitis disappearing; cures resulted in 40 cases, though here and there evidence of pulmonary tuberculosis was reported. The majority of cases were females, which may find its explanation in the fact that most were operated upon under error in the diagnosis of ovarian cyst. The most recent and comprehensive work on tuberculosis of the peritoneum, which has recently appeared from the pen of Vierordt ("Ueber die Tuberculose der serösen Häute," in *Zeitschrift f. klin. Medicin.*, Bd. xiii, Heft 2), should be consulted by those who wish to secure for reference an exhaustive treatise on this subject. The statistics are yet too meagre, the correctness of diagnosis not entirely above doubt, and the period of observation after operation not long enough; but, in view of the results, there is no longer any justification for expectant treatment. Even though in some cases recovery was not permanent, the fluid did not re-accumulate, and the patients were relieved of their distress. Spontaneous recovery from tubercular peritonitis is exceptional, and operative interference is indicated the more, as it would seem that, in many cases, tuberculosis of the peritoneum is a primary affection and the source of general infection. As all other therapeutic measures are of no permanent value in such cases, and laparotomy done under antiseptic precautions may be considered almost free from danger, the operation is certainly strongly indicated.

Pathology and Morbid Anatomy.—The effect of the bacillus of tuberculosis on the peritoneum is not uniform, and the conditions found in peritoneal tuberculosis are variable. Lindfors, in a clinical and pathological study, based on 109 recorded cases of peritoneal tuberculosis, divides the cases into seven classes. He states that the acute variety may assume the form of circumscribed, general, or suppurative peritonitis; in the chronic form there may be a free or encysted effusion, there may be simple adhesions, or the intestines may be so adherent as to cause intestinal obstruction. Lindfors thinks that the presence of acute or chronic pleurisy has an important bearing on the diagnosis of tubercular peritonitis. He is strongly in favor of laparotomy and the free use of iodoform within the peritoneal cavity. The conditions found in local tubercular peritonitis, in cases subjected to operative treatment and in examinations made in the post-mortem rooms, are such that all cases of this kind can be conveniently classified in three principal groups upon a pathological basis.

1. Tubercular Ascites.—The peritoneum is thickened, hyperæmic, and studded with masses of tubercle-tissue in the form of miliary nodules. The omentum is usually similarly affected. If the effusion is general, occupying the whole peritoneal cavity, the adhesions are few and slight. If the fluid is encapsulated the walls of the cavity are formed by intestinal loops, which are adherent among themselves and to the surrounding structures. The circumscribed form usually takes its origin from the floor of the pelvis, and often gives rise to a swelling which simulates an ovarian cyst to perfection. The fluid contained in the peritoneal cavity in the diffuse form, and in the confined space in the circumscribed variety, is either a clear, transparent serum, or serum in which small flocculi are suspended, or the fluid has become slightly turbid from the admixture of the products of retrograde tissue metamorphosis. The visceral peritoneum of the organs exposed to infection is in the same condition as the parietal peritoneum. Coagulation necrosis and caseation of the nodules appear to be retarded for a much longer time than in cases of glandular tuberculosis. The amount of fluid may vary from a teacupful in the circumscribed to 4 or 6 gallons in diffuse tubercular ascites. Secondary infection is found most frequently in the spleen, pleuræ, and lymphatic glands.

2. Fibrino-plastic Peritonitis.—In this form of tubercular peritonitis no fluid is found in the peritoneal cavity. The bacillus of tuberculosis produces a copious inflammatory product, and the peritoneal surfaces, which are studded with miliary tubercles, are covered by a thick layer of gelatinous fibrin, which cements together all the adjacent serous surfaces, so that the whole abdominal cavity appears to be filled with a large, boggy mass, composed of all the viscera adherent to each other, and with the inter-spaces between them filled with fibrin. The inflammatory product in these cases is rich in fibrin-producing substances, while the liquid transudation is either scanty or is absorbed as soon as it is poured out.

3. Adhesive Peritonitis.—In this variety of tubercular peritonitis the bacillus of tuberculosis exerts its pathogenic properties more on the fixed tissue-cells than the blood-vessels. The primary inflammatory exudation is slight, but the endothelial cells proliferate new tissue, which undergoes cicatrization, giving rise to firm and extensive adhesions. The plastic peritonitis may be so extensive as to cause intestinal obstruction from perfect immobilization of a large portion of the intestinal tract. In this, as well as in the foregoing form of tubercular peritonitis, ulceration of the intestine may take place, resulting in the formation of a bimucous, internal fistula, if the opening in two adjacent loops correspond, or the formation of a fæcal abscess with a subsequent fæcal fistula.

Symptoms and Diagnosis.—As tubercular peritonitis without effusion is not amenable to successful surgical treatment by laparotomy, nothing will be mentioned in reference to the diagnosis and treatment of the fibrino-plastic and adhesive varieties. Tubercular ascites is a chronic affection, especially when it occurs in the circumscribed form. Pain and tenderness are not prominent or even constant symptoms. The general health is at first but little impaired. Fever is slight or entirely absent. If the effusion is general, it comes on slowly, almost insidiously, as in ascites from other causes. From the absence of adhesions the fluid changes its location according to the position of the patient. If the patient is placed in the dorsal, recumbent position, the lumbar regions are dull on percussion; if placed on the side, the upper lumbar region is tympanitic, while the area of dullness on the opposite side is increased. In circumscribed tubercular peritonitis with encapsulation of the fluid, the swelling appears first either in the hypogastric or one of the iliac regions. The area of dullness does not change by placing the patient in different positions. In free ascites tuberculosis of the peritoneum should be suspected, if the ordinary causes of ascites, cirrhosis of the liver, valvular disease of the heart, and the presence of an intra-abdominal malignant tumor can be excluded. Circumscribed tubercular ascites might be mistaken for ovarian cyst, pregnancy, pyo- or hydro- salpinx, and pelvic abscess. Fluctuation is a symptom common to all of these conditions, and a differential diagnosis can only be made by a careful study of the clinical history and by a thorough examination. Pregnancy can usually be excluded by ascertaining the size of the uterus and by the presence or absence of the usual signs of gestation. A pyo- or hydrosalpinx can generally be recognized by bimanual exploration, especially if the examination is made, as it should be, under the influence of an anæsthetic. A pelvic abscess is always preceded by an acute suppurative para- or peri- metritis, attended by severe symptoms which are absent in tubercular peritonitis.

The greatest difficulty presents itself in differentiating between a circumscribed tubercular ascites and an ovarian cyst. So close is the clinical resemblance of these two affections that a positive diagnosis is almost impossible without the aid of an exploratory laparotomy, and, as both affections can only be treated successfully by abdominal section, it is sufficient for all practical purposes to narrow the diagnosis down to one of these, and reserve a positive diagnosis until the abdomen is opened.

Treatment.—The surgical treatment of tubercular peritonitis with effusion by laparotomy has yielded sufficiently satisfactory results to make it an established procedure in such cases in the future. A spontaneous cure is the exception; death from local extension of the disease and from general infection the rule. A case came under my observation during the last two years where I have every reason to believe that tubercular ascites disappeared spontaneously. The patient was a woman, 40 years of age, with a marked hereditary tendency to tuberculosis, several sisters having died of pulmonary tuberculosis. She is the mother of several children, the youngest being 6 years old. Two years ago she was brought to me by her family physician with the diagnosis of ovarian cyst. At that time the swelling was as large as a child's head, occupying the hypogastric and left iliac region. Fluctuation distinct; no pain and but little tenderness on pressure; menstruation regular. General health only slightly impaired. After a careful examination I coincided with the diagnosis, and advised an early operation. Soon after this time the swelling began to diminish in size and disappeared completely in the course of a year, but the general health, instead of improving, began to fail. After the disappearance of the swelling she began to suffer from a deep-seated pain at a point corresponding to the cartilage of the eighth rib on the left side, and in the course of a few months a fluctuating swelling appeared under the costal arch at that point. Tuberculosis of the ribs was suspected, but at the time of operation an encapsulated tubercular abscess was found in the abdominal cavity, to the left of the great curvature of the stomach and above the splenic flexure of the colon. A large quantity of liquefied, caseous material was evacuated. The wall of the abscess was lined with a thick layer of granulation tissue, which was thoroughly removed with a sharp spoon, and after irrigation the cavity was carefully dried and packed with iodoform gauze. The wound healed by primary intention, and the entire cavity closed in the course of four weeks without a drop of pus. The woman has since greatly improved in health, and is completely relieved of her pain. There can hardly be a question that the accumulation of fluid which was mistaken for an ovarian cyst was a limited ascites, caused by a circumscribed tubercular peritonitis, and that the infection in the upper portion of the abdominal cavity resulted from this, the primary depot. It is not at all improbable that, had an operation been performed at the time it was advised, this extension of the infection might have been prevented. The results obtainable by laparotomy in the two different forms of tubercular ascites are well shown by 2 cases which occurred in my practice during the last year.

The first patient was a girl, 17 years old, without a tubercular history. She had always been in good health until about a year ago, when she commenced to suffer from pain in the left iliac region, and soon after a perceptible swelling appeared in that locality, which gradually increased in size until the time I saw her, when it reached above the umbilicus and beyond the median line. Has never menstruated. Patient is anæmic and somewhat emaciated, but was never confined to bed. Examination reveals no disease in any of the important organs. Diagnosis of ovarian cyst had been made by several physicians. The abdomen was opened by a median incision, and a large quantity of clear, straw-colored serum escaped as soon as the peritoneum was incised. The parietal peritoneum, as well as the intestines, which [illegible] rt of the wall of the cavity, were studded with [illegible] llet-seed.

These nodules were largest and most numerous in the region of the left Fallopian tube, which, however, was normal in size. The cavity was dried and freely dusted with iodoform, and a Keith glass drain inserted as far as the floor of the space of Douglas. A large quantity of serum was removed from the tube for the first few days, when it became more and more scanty, so that the glass tube could be removed at the end of the second week. Through a small fistulous tract serum continued to escape for six weeks, when the fistula closed. The patient has gained 15 pounds in weight, and at this time, a year after the operation, is in perfect health, with no signs of a local return. That the peritonitis in this case was tubercular was demonstrated by an inoculation experiment. A nodule was removed from the peritoneum and implanted into the peritoneal cavity of a guinea-pig with a positive result. The second case was a woman, 42 years of age, without any history of tuberculosis in her family. She is the mother of a large family, the youngest child being 5 years of age. Her abdomen began to enlarge four months before she came under my care. Pain not severe, but gradual loss of flesh and strength. As no local cause for the ascites could be found, the abdomen was opened in the median line, and at least two pailfulls of clear serum escaped. The intestines and parietal peritoneum presented an exceedingly vascular appearance, and were studded with minute miliary nodules. These nodules, again, were largest in the pelvis, but both tubes were found in a normal condition. The same course was pursued as in the first case, and drainage was kept up for two weeks, when the flow of serum was so scanty that it was deemed advisable to remove the tube. The wound healed completely in a few days, and the patient left the hospital greatly relieved. The fluid, however, accumulated so rapidly that in two weeks she had to be tapped, and from this time on the patient could not leave her bed. The tapping had to be repeated every two weeks. Symptoms of pulmonary phthisis developed soon after she left the hospital, and death from general miliary tuberculosis occurred in less than three months after the operation. The danger of re-accumulation of fluid and general infection is much greater in diffuse tubercular peritonitis than in the circumscribed form, as in the latter the area of infection is more limited, and general infection is less likely to occur on account of the presence of a wall of plastic material which surrounds the tubercular field. In operating for circumscribed tubercular ascites it is very important to exercise great care in opening the abdominal cavity, as a loop of adherent intestine may be found at the point where the incision is made. The peritoneum must be recognized and carefully divided in order to prevent wounding of the bowel, should such a condition be met with. Iodoformization of the cavity is one of the important indications of treatment. Drainage must be maintained until accumulation of serum in the tube has ceased. Uniform equable compression of the abdomen with strips of adhesive plaster or a well-fitting bandage should be kept up throughout the entire after-treatment. In cases where a well-defined local tubercular focus is found, which we have reason to regard as the cause of the peritonitis, this should be removed or rendered harmless by appropriate treatment.. A tubercular Fallopian tube should be removed if this can be done. Other caseous foci are removed with a sharp spoon, or they can be destroyed or rendered harmless by igniquncture and thorough iodoformization.

CHAPTER XX.

TUBERCULOSIS OF BONES AND JOINTS.

TUBERCULOSIS OF BONE.

NEXT to the lungs and lymphatic glands the bones are most frequently the seat of tubercular infection. Tuberculosis of the bones is an exceedingly frequent affection in children and young adults. Its favorite location is in the epiphyseal extremities of the long bones, although it is also quite frequently met with in the short bones of the carpus and tarsus and some of the flat and irregular bones, as the ribs, scapula, ileum, and vertebræ.

Embolic Infection the Cause of Osseous Tuberculosis.—Practically, direct tubercular infection does not occur, and when the disease has made its appearance it is only an evidence of the existence of a tubercular focus in some other organ. We observe clinically, what Mueller has demonstrated experimentally, that, when the bacilli of tuberculosis are present in the blood-current, very often localization takes place near the epiphyseal cartilage in young persons by the microbes becoming arrested in one of the terminal branches of an artery, the lumen of which becomes obliterated by the presence of a minute embolus of granulation tissue containing bacilli; or the lumen of the vessel is gradually diminished by the formation of a mural thrombus, which forms around bacilli implanted upon the vessel-wall, and the lumen of the vessel is finally completely obstructed by the growth of the thrombus.

The new vessels in the vicinity of the centres of growth in the bones of young persons, on account of their imperfect structure and irregular contour, furnish the most favorable conditions for the arrest of floating granular matter and the localization of pathogenic microbes. The predisposing anatomical element goes far to explain the frequency with which we meet with tubercular foci in the epiphyseal extremities of the long bones.

The following table, prepared by Schmallfuss, gives a good idea of the relative frequency with which different bones are affected with tubercular lesions:—

BILLROTH.	JAFFE.	PER CENT.	SCHMALLFUSS.	PER CENT.
Vertebra.	Vertebra.	26	Knee.	23
Knee.	Foot.	21	Foot.	19
Cranium and Face.	Hip.	13	Hip.	16
Hip.	Knee.	10	Elbow.	9
Sternum and ribs.	Hand.	9	Hand.	8
Foot.	Elbow.	4	Vertebra.	7.5
Elbow.	Pelvis.	3	Tibia.	4
Pelvis.	Cranium.	3	Cranium.	4
Tibia, Fibula, and Femur.	Sternum, Clavicle, and Ribs.	3	Pelvis.	3.6
			Sternum, etc.	3.6
Shoulder.	Shoulder.	2	Femur.	1.9
	Femur.	1	Shoulder.	1.5
Humerus.	Tibia.	1	Ulna.	1.4
Ulna.	Fibula.	1	Humerus.	1
Radius.	Humerus.	1	Radius.	0.7
Scapula.	Scapula.	0.6	Fibula.	0.5
	Ulna.	0.6	Patella.	0.1

It is safe to state that before puberty the primary lesion in tubercular affections of joints is located in one or both of the epiphyses of the bones which enter into the formation of the joint, while in the adult primary tuberculosis of the synovial membrane is of more frequent occurrence. As age advances and the process of ossification is completed, the predisposing localizing causes in bone apparently disappear, while the synovial membrane becomes more susceptible to primary localization. Of 204 specimens of tubercular joints obtained from patients of all ages, examined by Mueller, 158 were primary osteal, and 46 primary synovial, tuberculosis.

Artificial Tuberculosis of Bone Produced by Direct Intra-vascular Infection.—Wm. Mueller, formerly one of König's assistants, produced the characteristic clinical form of tuberculosis in bone experimentally by injecting tuberculous material into the nutrient artery of long bones. König for a long time had claimed that the wedge-shaped sequestrum, so constantly found in tubercular foci in the articular extremities of the long bones was due to occlusion of a small artery by a tubercular embolus. Mueller's experiments were undertaken to produce this condition artificially. He made 16 experiments on rabbits, injecting tuberculous pus into the femoral artery, some in a peripheral, some in a central direction, without any positive results following. In a second series the same material was thrown directly into the nutrient arteries of the femur and tibia. Of 10 of these cases 2 showed a tuberculous focus in the medulla of the diaphysis of the tibia; in another case miliary tuberculosis in the femur and tibia, and in the latter bone a small caseous nodule in the spongy part which contained numerous bacilli. The animals were killed eight weeks after injection, and showed no evidences of organic disease except a few tubercles in the lungs. Twenty experiments were made on young goats, 5 on sheep, and 2 on dogs. The tuberculous material was injected directly into the nutrient artery of the tibia, the tibial artery being tied above and below the junction with this vessel. Primary union of the wound was obtained in all cases except in one dog. In the dogs and sheep all experiments resulted negatively. In the goats bone affections were produced that were identical with tubercular bone-lesions found in man. Most frequently the disease was established in the diaphysis, cheesy masses and granulation tissue showing themselves in the medulla and cortical portion of the bone, or tuberculous osteomyelitis with or without sequestration. Typical lesions were also found in the ends of the bones, with and without implication of the adjacent joints. In 2 of these cases the epiphysis was affected, while in 3 the shaft was involved. The following experiment made by him furnishes a good illustration of the identity of the bone disease produced experimentally with the disease as it occurs in man.

Tuberculous material was injected into the tibial artery of a goat 3 months old. Wound healed in eight days. Some lameness four months later, gradually increasing during the next nine months. At the same time a swelling appeared at the knee-joint. Tibia painful on outer side. Animal killed thirteen months after the injection. At the necropsy there was found a typical fungous disease in the knee-joint, most advanced at the lateral aspects of the joint; a wedge-shaped sequestrum in one of the tuberosities of the tibia, a small granulation mass in the centre of the head of the tibia, and two similar granulation masses in the lower epiphysis of the femur. Excepting the lymphatic glands of the knee-joint, no other organs were affected. In some of the cases, pulmonary tuberculosis, twice general miliary tuberculosis. The remainder of the animals were killed when they began to show lameness—fourteen days to thirteen months after infection. The tubercular lesions thus produced were examined for bacilli, and these were never found absent. The starting-point, in every instance, must have been a tubercular embolus in one of the ultimate minute branches of the nutrient artery near the epiphyseal extremity of the bone.

Clinical and Bacteriological Researches.—Schuchardt and Krause examined a great variety of tubercular lesions, and came to the conclusion that tubercle bacilli can be found in them without exception, but, as a rule, few in number, and often only to be detected after long and patient search. They found them invariably present in cases of secondary and primary tuberculosis of synovial membranes, tuberculosis of bone, in tubercular abscesses. and in the latter cases not in the fluid contents, but in the granulations lining the abscess-wall. Renken found the bacillus of tuberculosis in all cases of spina ventosa which he examined. Mueller carefully studied numerous specimens of synovial and bone tuberculosis, with special reference to the existence of the bacillus of tuberculosis, and, although the results in a number of cases were negative, he believes that the most intimate and direct etiological relations exist between the bacillus and all tubercular lesions in bones and joints. Among others who have shown the never-failing presence of the bacillus in different forms of surgical tuberculosis, including bones and joints, may be mentioned Kanzler, Mögling, Bouilly, and Letulle. Tuberculosis of bone and fungous disease of joints, like lymphatic tuberculosis, have been, and by some are still, regarded as scrofulous affections. Kanzler wished to make a distinction between scrofula and tuberculosis, as he found the bacilli not as constant in the former, and observed that, after implantation of tissue of what he regarded as scrofulous affections in animals, the process was slower than after inoculation with the products of recognized forms of tuberculosis. Letulle considers scrofula and tuberculosis as belonging to one and the same disease, of which the former constitutes the milder form, and appearing externally, while the latter represents the graver form, attacking by preference the internal organs. The points made by the last two authors are too unimportant for further consideration as a scientific, or even practical, distinction between scrofula and tuberculosis as applied to affections of the bones or any other organs. *The surgeon must recognize every lesion as tubercular in its origin, nature, and course in which the bacillus of tuberculosis can be found, from which successful cultivations can be made, and with which the disease can be artificially produced in animals by inoculation.* The presence of the bacillus of tuberculosis in the body and its localization in the medullary tissue of bone is the *conditio sine quâ non* in the causation of osseous tuberculosis. The influence of traumatism in the etiology of tuberculosis of the bones and joints has been greatly overestimated. Traumatism as an etiological factor occupies a subordinate rôle, inasmuch as it only proves, at least, as an exciting cause in persons already infected with the essential cause. Max Schüller proved experimentally in animals infected with tuberculosis (for instance, through the respiratory tract) that a slight traumatism to a joint would determine localization of the microbes floating in the blood-current in the part injured, and that a tubercular synovitis or pararthritis would follow.

Clinically, tuberculosis of the bones can be traced only in a small per cent. of the cases to a traumatic origin. It is, as Volkmann asserted long ago, characteristic that the traumatism is always slight, often quite insignificant; tuberculosis of bone, even in tubercular subjects, seldom, if ever, follows a fracture, as the injury in such cases is productive of such active cell proliferation that will neutralize the pathogenic action of the bacilli, which might reach the seat of injury with the extravasated blood. It is also possible that in many cases, at least, the attention of the patient or his friends is first accidentally called to an existing tubercular focus by the immediate effects of the injury, the latter having had no influence in the causation of the disease. Every child large enough to run around injures himself more or less (almost) daily, and yet tuberculosis of the bones and joints follows as a consequence only in comparatively few, and in such cases the essential cause must be present in the blood or tissues at the time the injury is received. As has been previously stated, what is generally regarded as local bone tuberculosis (by which we mean the absence of recognizable tubercular lesions in other organs) is in reality a secondary disease, resulting from the introduction of bacilli through the respiratory or alimentary tract into the circulating blood, with localization in the bone, or the entrance of bacilli into the circulation from a pre-existing but undetectable tubercular product with secondary localization in bone. In this sense a primary, or, to use a more correct expression, a localized osseous or articular tuberculosis is, according to Kummer, found in about 40 per cent. of the cases; in the remaining 60 per cent. depots are found at the same time in other organs of the body; the lung comes first, with 25 per cent.; other joints, 10 per ceht.; other bones, 10 per cent.; lymphatic glands, 10 per cent.; peritoneum, 3 per cent.; pleura, 2 per cent.

Pathology and Morbid Anatomy.—The tubercle bacillus has a distinct predisposition for the medullary tissue of the bones, and especially for the red medullary tissue in the cancellated tissue in the region of the epiphyseal cartilage of the long bones. As an inflammatory affection it is more correct to speak of tuberculous osteomyelitis than tuberculosis of bone, since the medullary tissue and the blood-vessels which it contains are the parts that take an active part in the inflammatory process. The anatomical conditions of the vessels in the epiphyseal region of the long bones in young persons, and in the vessels of the medullary tissue, favor implantation of the microbes upon the vessel-wall, and they also explain the frequency with which localization of the tubercular process takes place in this locality. The shaft of the long bones is generally exempt from tubercular disease, with the exception of the phalanges of the fingers and toes, and the metacarpal and metatarsal bones in children, where the tuberculous osteomyelitis gives rise to the well-known *spina ventosa* of the old authors. As soon as embolic infection in bone has taken place, a pro [illegible] is and decalcification occurs around the tubercular embolus or thrombus, and the pre-existing medullary and connective tissues are transformed into embryonal or granulation cells, which imparts to the product of the specific inflammation its characteristic fungous appearance. It is not often that only a single focus of tubercular infection in bone is present; more frequently two or three foci appear in the same region simultaneously or in slow or rapid succession, and it is not unusual to find that two neighboring epiphyses are infected at the same time or during the course of the disease. In bone the granulation tissue undergoes the same series of secondary degenerative tissue changes as in the lymphatic glands; hence, in advanced cases we expect to meet with caseation, liquefaction of the cheesy material, and suppuration in cases of secondary infection with pyogenic microbes. The obstruction of a small artery by an embolus or thrombus which contains tubercle bacilli usually leads to necrosis and sequestration of a triangular piece of bone, which, in its outlines, marks the area of tissue which received its blood-supply from the obstructed vessel; thus the triangular sequestra are formed that are so frequently met with in osteal tuberculosis of the epiphyseal extremities. If the embolus is located on the side of the epiphyseal cartilage toward the joint, the base of the triangular sequestrum is directed toward the joint, and not infrequently projects slightly into the joint. It is seldom that tuberculosis of bone develops in the course of pulmonary tuberculosis, but pulmonary and diffuse miliary tuberculosis can be traced frequently to a tuberculous osseous focus. The intimate relations which exist between the tubercular nodule in bone and the blood-vessels furnish a satisfactory explanation of the frequency with which systemic infection takes place. A person once infected with the bacillus tuberculosis is liable to suffer from the different forms of localized tuberculosis, and finally dies of pulmonary or general miliary tuberculosis. Volkmann has well said that a child suffering from glandular tuberculosis has a good chance to become the subject of osseous tuberculosis during adolescence, and to die of pulmonary tuberculosis before reaching the age of 30. As soon as the granulation process in bone reaches an adjacent vein, the tissues constituting the vein-wall undergo the same process, the bacilli reach the lumen of the vessel and re-enter the systemic circulation, and give rise to miliary tuberculosis in organs which are anatomically predisposed to secondary infection. As long as decalcification of the surrounding bone goes on the infection is progressive, but as soon as osteosclerosis takes its place the process becomes limited; the microorganisms are shut in, as it were, by an impermeable wall of sclerosed bone. The most unfavorable conditions are created in cases in which the tubercular focus becomes the seat of a secondary infection with pyogenic microbes, as the suppurative process opens up to the bacillus of tuberculosis new areas for invasion, in which the resistance of the tissues to tubercular infection has already been greatly diminished. It is also during the suppurative stage that joint complications are most likely to arise. The clinical history of cases of tuberculosis of bone, as well as the macroscopical and microscopical appearances of the lesion, are typical of tuberculosis as found in other organs. The crucial test which proves the tubercular character of most of the chronic inflammatory affections of bone in children has been furnished by bacteriological investigations and experimental research. Most of the investigators who have studied this subject agree that in tubercular bone affections it is sometimes very difficult to find the bacillus, that it is not found in great abundance, and that sometimes it has evaded even the most careful search. According to König, who is authority on everything that pertains to tuberculosis of bones and joints, all cases of osteo-tuberculosis can be arranged under four principal groups, according to the predominating pathological conditions of the lesions: 1. The granulating focus. 2. The tubercular necrosis. 3. The tuberculous infarct. 4. Diffuse tuberculous osteomyelitis.

1. The granulating focus is found as single or multiple, round or oval cavities, from the size of a millet-seed to that of a pea or hazel-nut, containing living embryonal tissue, or, if this has been destroyed by coagulation necrosis and caseation, a yellowish-gray, cheesy material, or liquid tuberculous pus. Minute spiculæ of bone are imbedded among the granulations or suspended in the liquefied caseous material. Histologically, the granulation material is composed of the same cell-elements as recent tubercle in other organs, only that, as a rule, the giant cells are more numerous and of larger size. If caseation has taken place, the cheesy material is surrounded by a zone of granulation tissue. As long as the process has not come to a stand-still, the surrounding bone is osteoporotic, and can be easily scraped out with a sharp spoon. As soon as the inflammatory process has subsided the osteoporotic bone becomes sclerosed, and the tubercular focus is walled in and, for the time being, is rendered harmless. Cheesy tubercular cavities in bone resemble the same condition in the lungs, only that secondary infection with pus-microbes is of less frequent occurrence, and on this account the cavity never attains such large size as in the latter organ.

2. Tubercular necrosis necessarily follows if the infected area exceed the size of a hazel-nut. The non-vascular structure of the tubercular product and the blocking and destruction of blood-vessels during the early stages of the tubercular inflammation produce early death of the bone, corresponding to the limits of the inflammation, and if this exceed

the resorption capacity of the granulation tissue the dead tissue is not removed by absorption, and is found as a sequestrum as soon as it has become detached from the surrounding healthy bone. If the tubercular process has been rapid and the granulation tissue is scanty, the necrosed bone is not osteoporotic; but if the disease has pursued a more chronic course, and has resulted in the production of an abundance of granulation tissue, it presents a honey-combed appearance, is irregular in shape and in size, does not correspond with the area of the infected district, as part of it has been absorbed by the granulations. Its color depends on the condition of the granulations which surround it; if these have not undergone secondary degenerative changes it may resemble healthy bone, but if caseation has taken place it is infiltrated with the cheesy material, and then presents a grayish-yellow or yellow appearance. If the necrosed bone has undergone no reduction in size, and the granulations surrounding it are few, it remains firmly wedged in position, and under such circumstances it is often difficult to locate the exact boundary-line between it and the surrounding healthy bone or to dislodge it from its position.

3. The tuberculous infarct is only another form of tubercular necrosis, and is separately classified because the necrosed bone is always wedge-shaped, and the necrosis has been caused by the impaction of an embolus containing tubercle bacilli in a distal branch of a nutrient artery. The size of the vessel obstructed by an infected embolus will determine the extent of the necrosis. If the embolus is small, the area of necrosis may be increased by the blocked vessel becoming the seat of secondary thrombosis, obliteration of the vessel taking place in a proximal direction by growth of the thrombus toward the heart. As the cortical portion of the bone is seldom involved by a tubercular infarct, the necrosed area is often overlooked in operations on tubercular joints unless the bone is sawn through. If the base of the wedge-shaped piece project into a joint that has been used, its surface will be found smoothly polished by the movements in the joint. Separation of the sequestrum takes place more slowly than after suppurative osteomyelitis, the process requiring often, according to the size of the sequestrum and the activity of the inflammatory process, months and years for its completion. If the granulations which surround the sequestrum do not undergo cheesy degeneration, the bone becomes imbedded, and fits accurately into the cavity, and if the surrounding zone of granulation is converted into connective tissue it may become permanently encapsulated; but even from such an apparently healed depot local and general infection can occur at any time.

4. The diffuse form of tuberculous osteomyelitis is quite rare. The

pathological and clinical characteristics of this form of local tuberculosis consist in the rapid local extension of the affection and the danger to life from general infection. On making a longitudinal section through a long bone affected by diffuse tuberculous osteomyelitis, we observe conditions which closely resemble acute suppurative osteomyelitis. We find large, irregular, often multiple areas of a yellowish-white infiltration with multiple foci of liquefied cheesy material. The infection extends, as in cases of suppurative osteomyelitis, along the blood-vessels and Haversian canals to the periosteum, resulting in diffuse plastic osteomyelitis with the formation of irregular, diffuse masses of bone. In these cases there is no tendency to limitation in the formation of sequestra, but rather a tendency to spread indefinitely, and to invade even the medullary tissue of the shaft. Patients suffering from this form of tubercular osteomyelitis are exposed to the dangers of a fatal general tuberculosis if the infected tissues are not removed by a timely and thorough operation. In operating it is important to recognize this form, since it requires more radical measures,—either amputation or very extensive excisions of the entire thickness of the affected bone. Local operations such as will meet the indications in the other varieties of osteo-tuberculosis are of no avail. With the exception of this form of tuberculosis of bone the periosteum seldom participates in the tubercular inflammation. When the dry granulation form reaches the periosteum, a small, soft, elastic, limited granulation swelling forms,—first under the periosteum, later outside of it. It is characterized by slow growth, comparatively little pain, slight tenderness, and a tendency to remain stationary for a long time. If, however, the central focus has become cheesy, and the liquefied cheesy material comes in contact with the periosteum and the paraperiosteal tissues, a large tubercular abscess forms in a short time. As soon as the periosteum has been perforated the cheesy material infects the connective tissue, which then takes an active part in the formation of the tubercular abscess. Before such an abscess spontaneously ruptures, the skin overlying it becomes tuberculous and presents, at the point of perforation, the appearance of lupus.

Symptoms and Diagnosis.—The general symptoms are often no indication of the existence or extent of the local disease, as patients with quite extensive osteo-tuberculosis may present every appearance of perfect health. More than ten years ago König called our attention to the fact that a slight rise in the temperature is frequently present even in cases of limited local tuberculosis. If the thermometer show a normal morning temperature, but a slight rise toward evening, if not more than half a degree Fahrenheit, but continued for weeks, it indicates a careful search for a local tu[illegible]ocus. Progressive anæmia is always an unfavorable symptom, as it indicates either the presence of additional foci in important organs or accompanies the exhaustive purulent discharges after secondary infection with pus-microbes. The occurrence of mixed infection, with or without a direct infection-atrium, is usually announced by a high temperature and other symptoms of septic infection. The local symptoms vary according to the location, condition, and size of the tubercular focus and the presence or absence of complications.

1. Pain.—Pain is an almost constant symptom, but its intensity is subject to great variation. Unlike in acute suppurative osteomyelitis, the inflammatory product does not give rise to the same degree of tension; hence pain is not so severe. The primary exudation in tubercular inflammation is always scanty, and the inflammatory product is composed mostly of granulation tissue derived from pre-existing cells; at the same time the surrounding bone-tissue becomes osteoporotic, consequently tension is to a great extent avoided and pain is either slight or entirely absent. Children suffering from spina ventosa complain of little pain, although a phalanx of a finger may be almost completely destroyed by a tubercular osteomyelitis. In such cases the granulation tissue is formed slowly, the compact layer of the bone is rendered osteoporotic, and generally yields to the intra-osseous pressure and expands perhaps to twice its normal thickness; pain is slight or entirely absent, because no great intra-osseous tension has occurred. That tension or pressure greatly aggravates pain in osseous tuberculosis is one of the most familiar facts in surgery. Pain is promptly relieved in a case of tubercular spondylitis by suspension and rest in the recumbent position, and greatly aggravated by flexion of the spinal column, which necessarily produces pressure upon the bodies of the inflamed vertebræ. In osteo-arthritis of the large joints pain is relieved by rest and extension, and is always increased by use of the limb or by pressing the inflamed articular surfaces against each other. It may be stated, as a rule, that the intensity of the pain bears a direct relationship to the acuteness of the inflammatory process. The pain is intermittent and more severe during the night. The nocturnal exacerbation of the pain, as evidenced in children by restlessness during sleep, moaning, grinding of teeth, and horrible dreams, is often one of the first symptoms which excites suspicion of the existence of osteo-tuberculosis. The pain is not always referred to the seat of lesion. Tubercular osteomyelitis of the head and neck of the femur gives rise to pain in the region of the knee-joint, and children suffering from tuberculosis of the spine usually refer all the suffering to the pit of the stomach or to some other part of the abdomen supplied with nerves that take their exit from the spinal canal at a point corresponding to the inflamed vertebra.

2. Tenderness.—The existence of tenderness over a point corresponding to the tubercular focus in the interior of a bone is one of the surest indications of the existence of osteo-tuberculosis. In many cases of epiphyseal tuberculosis patients have been treated for some supposed lesion in the adjacent joint, simply because this symptom was not carefully searched for, or, if discovered, its significance was misinterpreted. In such cases the existence of a circumscribed point of tenderness in the epiphyseal line and the absence of lesions in the joint will enable the surgeon to locate accurately a focus in the interior of a bone. If more than one focus is present in the epiphyseal extremity of a long bone the number of tender points will correspond with the number of foci in the bone. Whether a central focus in a bone could be always recognized by relying upon this symptom is somewhat doubtful, but usually the foci are located sufficiently near the surface of the bone to give rise to tender points, which can be readily located by finger pressure.

3. Swelling.—External swelling is absent until the atrophic layer of compact bone yields to the intra-osseous pressure, as may be seen in advanced cases of spina ventosa, or until by pressure atrophy over the centre of the focus the compact layer is perforated, and a soft, circumscribed, boggy swelling forms underneath the periosteum. If the granulation tissue has retained its vitality the extra-osseous swelling increases very slowly in size, and there is no tendency to diffuse infection of the connective tissue after the granulations have reached the paraperiosteal tissues. Pseudo-fluctuation is generally present, and many such granulating foci at this stage have been carelessly incised under the mistaken diagnosis of abscess. If the central focus has undergone caseation before the periosteum is perforated, then the paraperiosteal tissues become rapidly infected, and a tubercular abscess, such as has been described before, develops in a short time. The abscess wanders away from the place where it originated in directions offering the least resistance, along preformed anatomical spaces and in obedience to the law of gravitation. The size of such an abscess is, absolutely, no indication of the extent of the primary lesion in the bone, as a minute focus may be the cause of a large abscess, and a small abscess may mark the location of an extensive primary lesion. Œdema is usually not well marked, even if the abscess is large, unless secondary infection with pyogenic microbes has occurred. The diffuse form of tuberculous osteomyelitis is always attended by a plastic osteomyelitis, and, consequently, the early appearance of external swelling is one of the points to be taken into consideration in differentiating between the different forms of osteo-tuberculosis. The swelling that attends tuberculosis in bones deeply seated, as the vertebræ, hip-joint, and pelvic bones, does not become apparent until the existence of a tubercular abscess indicates the probable seat of the primary lesion.

4. Redness.—The skin over a tubercular focus in the interior of a bone or over a tubercular abscess presents a normal appearance until it has become infected and shows other unmistakable signs of tuberculosis. This does not occur until the granulations have permeated the deeper portions of the skin, or until the caseous material has only the skin for its covering. Under such circumstances the skin presents a dusky-red hue, owing to impaired capillary circulation, and becomes more and more attenuated by pressure atrophy and destructive changes until it finally yields to the pressure atrophy from beneath, and spontaneous evacuation of the contents of the abscess takes place. If the subcutaneous product is composed of granulation tissue the undermined skin, after putrefaction has taken place, is destroyed by degrees and the part presents the appearances of lupus.

5. Atrophy of Limb.—Muscular atrophy is almost a constant symptom in osteo-tuberculosis as well as in tubercular synovitis. This atrophy is not caused altogether by inactivity of the limb, and it appears to be due to tropho-neurotic lesions.

Besides a careful study of the clinical history, several diagnostic measures may be resorted to in doubtful cases to enable the surgeon to make a positive diagnosis.

Means of Differential Diagnosis—(a) Akido Peurastik.—Exploration of a doubtful swelling with a strong steel needle was introduced by Middeldorpf, for the purpose of ascertaining the consistence and probable structure of the tissues composing the swelling. He called this simple procedure *akido peurastik*. The presence of a tubercular focus in the interior of a bone can often be demonstrated by this aid to diagnosis before any external swelling has appeared. A strong needle of a hypodermic syringe can be used for exploring a bone the density of which has been diminished by chronic inflammation, if this latter has not been followed by osteosclerosis. During the active stage of osteotuberculosis the bone for a considerable distance around the focus is osteoporotic, and can be readily penetrated by a strong, sharp needle. The exploration should be made under strict antiseptic precautions. The puncture is made in the centre of the tender area, and in a direction corresponding to the probable location of the central focus. If the needle meet with any considerable resistance in the bone, it is advanced by rotatory movements; the arrival of the point in the granulating centre or caseous focus is announced by a sudden loss of resistance. By advancing the needle sufficiently to touch the opposite side of the cavity its probable size can be ascertained.

(b) Exploratory Puncture, with Aspiration.—If the needle of an exploratory or hypodermic syringe is used to make the akido peurastik, exploration of the bone may be followed by removing some of the contents of the cavity for examination by aspiration. If the tubercular product has undergone caseation and liquefaction some of the cheesy material can be removed by aspiration, and the nature of the lesion may then be revealed by positive demonstration. If still further evidence is required, a guinea-pig may be inoculated with the same needle, which still contains enough of the material to produce a positive result in the animal. If the cavity contain granulation tissue little fragments of this can be drawn into the needle, and with these inoculation experiments for diagnostic purposes can be made. In tubercular necrosis it may be possible to detect the presence of the sequestrum and ascertain its mobility by exploratory puncture. If a tubercular abscess has formed, the character of the contents of the swelling may be ascertained by using the exploratory syringe, and the nature of the primary cause demonstrated, if need be, by injecting the material aspirated into the subcutaneous tissue or peritoneal cavity of a guinea-pig. In the differential diagnosis of tuberculosis of bone, it is necessary to exclude synovial tuberculosis, sarcoma, echinococcus-cyst, rachitis, suppurative osteomyelitis, and syphilis. Many cases of primary tuberculosis of bone have been mistaken for synovial tuberculosis, and *vice versâ*. Primary tuberculosis of bone frequently results in contractures of joints without direct implication of the joint, and this has often led to a wrong diagnosis. In primary synovial tuberculosis the first pathological changes occur in the joint, and no tender points will be found in the epiphyseal regions. In osteo-tuberculosis not complicated by an extension of the disease to the adjacent joint, the first symptoms are referred to the lesion existing in the interior of the bone, and it is usually not difficult to ascertain the existence of circumscribed points of tenderness which correspond to the location of the foci. Periosteal sarcoma is from the beginning an extra-osseous product. Central sarcoma, as a rule, increases more rapidly in size than a tubercular swelling, and is often the seat of pulsations and a blowing sound which can be heard by auscultation. Central sarcoma is often the cause of a pathological fracture, while this accident is exceedingly rare in osteo-tuberculosis. Echinococcus of bone is an exceedingly rare affection, but, as it may simulate osteo-tuberculosis, differential diagnosis must be based on an exploratory puncture, which will yield a clear serum containing the characteristic hooklets in the former instance, and granulation tissue or the products of caseous degeneration in the latter. Rachitis gives rise to swelling and pain in the epiphyseal regions; but this affection is not limited to one or two bones, and affects almost every bone in the body alike. Epiphyseal multiple osteomyelitis is an acute or, at least, subacute affection, and results early in the formation of purulent foci, and is often attended by epiphyseolysis. The virus of syphilis has a special predilection for the periosteum, while this structure is almost immune to primary tubercular affections. In 95 out of every 100 cases chronic inflammation in bone means tuberculosis, and, unless there are special reasons which should render the diagnosis doubtful, it is safe to adopt a treatment adapted for tubercular osteomyelitis in almost every case where the symptoms point to a chronic inflammation and the existence of a tumor or parasitic growth can be excluded.

Prognosis.—On the whole, the prognosis is more favorable in cases of osteo-tuberculosis than if the tubercular infection is located in the skin, a joint, lymphatic gland, or any of the internal organs. Spontaneous healing of a tubercular focus in bone is possible under favorable conditions. Everything that adds to the patient's strength and power of resistance to the microbic infection adds to the possibility of such a favorable termination. If the patient is well nourished, and, above all, if the blood is in a normal condition, limitation of the disease may occur before caseation has taken place; and if cheesy material has formed, and it can be removed by operative interference, the prospects of a permanent recovery are good. It must be, however, admitted that every person who has suffered from an attack of osteo-tuberculosis during childhood or youth, even if an apparent perfect cure has been effected spontaneously or by operative measures, is always in danger of becoming the subject of re-infection at any subsequent time. The spores of the bacillus of tuberculosis may remain in a latent condition for an indefinite period of time in the cicatrized primary lesion, to become a cause of subsequent danger as soon as the local or general conditions enable them to exercise their pathogenic properties. Healing by cicatrization is possible in the small granulating foci so long as the coagulation necrosis is limited and no caseation has occurred. In such cases the embryonal cells are converted into permanent connective tissue and the small fragments of bone are removed by absorption, while the bone around the cicatrix becomes sclerosed. If caseation has occurred, but the cheesy material has not undergone liquefaction, encapsulation of the tubercular product can take place by the wall of granulation tissue lining the cavity becoming converted into cicatricial tissue, forming a capsule, which, for the time being at least, mechanically prevents the local extension of the disease. Small sequestra may become imbedded in a connective-tissue capsule in a similar manner. If the sequestrum is large, it will act like every other foreign infected body, and sooner or later require an operation for its extraction. If the tubercular process has extended to a joint, the prognosis is more grave, and the chances for a spontaneous recovery are much diminished. The prognosis is always more grave, other things being equal, if the bone affected is so located that removal of the primary focus by operative treatment is anatomically impossible. The danger to life and the probability of local extension are always greater if the granulation tissue has been destroyed by coagulation necrosis and caseation, as the granulation tissue is one of the means by which regional and general infection are prevented. The danger to life is imminent if a large tubercular abscess has become infected with pus-microbes, as the secondary infection results in destruction of the granulation tissue lining the cavity, which favors the local and general extension of the tubercular infection and at the same time brings sepsis, exhaustion from profuse suppuration, and amyloid degeneration of important internal organs as additional elements of danger. The prognosis is always more grave in persons advanced in years than in children, as limitation of the disease occurs more frequently in the latter.

Treatment.—The medical treatment in patients suffering from osteotuberculosis must be tonic and supporting. Dietetic and hygienic treatment is of more value than the administration of drugs. Sea-bathing and change of climate will often accomplish more than bitter tonics, iron, quinine, arsenic, and codliver-oil. The local treatment, short of a radical operation, must consist in the use of such means as will aid the natural resources in effecting limitation of the tubercular process, of which the most important is

I. Physiological Rest.—The importance of securing for the inflamed part, as near as can be done by mechanical support, absolute physiological rest cannot be overestimated. The process of repair in a tubercular focus often meets with great and insurmountable difficulties. The embryonal cells, of low vitality almost from the beginning, are poisoned as soon as born with the ptomaines of the bacillus of tuberculosis, and consequently are converted into tissue of a higher type only under the most favorable conditions. The non-vascularity of the tubercle is another cause why the inflammatory product so seldom takes an active part in the process of repair. The first indication in the treatment of a tubercular osteomyelitis is to secure for the part a favorable condition of the circulation, which can only be done by securing rest. The most efficient way to procure rest, not only for the diseased part, but for the entire body, is to confine the patient to bed; but, as these affections are noted for their chronicity for months and years, enforced rest by this method would seriously impair the general health, and on this account it is advisable, in the majority of cases, to resort to one of the numerous mechanical appliances which will immobilize the part; while, at the same time, the patient can avail himself of the benefits to be derived from out-door air and change of scenery and surroundings.

In tuberculosis of the spine Sayre's plaster-of-Paris jacket, applied while the patient is partly suspended, answers a more useful purpose than any of the numerous complicated apparatuses which have been as yet devised. To apply the jacket properly requires a great deal of experience and the exercise of considerable skill. In many communities this method of treatment has become unpopular, both among physicians and the laity, from the bad results caused by improper application of the jacket. Hyperextension must be avoided, and the patient must be instructed to extend himself only until pain is relieved, and not beyond this point. The bony prominence at the seat of curvature must be carefully protected against pressure by applying on each side a pad sufficiently thick to prevent contact of the projecting spinous processes with the plaster cast. The plaster bandages themselves must be applied smoothly, so that after extension is removed the jacket will closely fit the unequal surface of the body. Another matter of great importance is to see the patient from time to time, in order to determine whether the jacket causes injurious pressure at any point, which, if this should be the case, is remedied at once, either by cutting out that portion of the jacket which has caused the decubitus or by applying a new one. In tuberculosis of any of the bones of the extremities rest can be secured most efficiently by immobilizing the limb in a plaster-of-Paris dressing. The splint must always include one or more of the adjacent joints. Undue constriction of the limb is prevented by interposing between it and the splint a thin layer of salicylized cotton. If the disease affect any of the bones of the lower extremities the patient must not be allowed to walk without crutches.

2. Ignipuncture.—During the early stages of osteo-tuberculosis excellent results have been obtained by ignipuncture,—a method of treatment devised a few years ago by Richet. If a tubercular focus can be accurately located, this method of treatment should receive a trial, as it is not attended by any risks and frequently effects a permanent cure. The field of operation is thoroughly disinfected, and, with the needle-point of a Paquelin cautery heated to a dull or red heat, the soft tissues and bone are perforated. In making the perforation it is necessary to advance the point slowly, and to remove it from time to time, and revive the heat in order to prevent impaction of the point. The entrance of the instrument in the cavity can be readily felt, as resistance at that moment is suddenly diminished. The therapeutic effect of ignipuncture is threefold: 1. The tunnel made establishes free drainage, and relieves promptly the intra-osseous tension. 2. At least a portion of the infected tissue is destroyed by the heat. 3. A plastic osteomyelitis is excited in the vicinity of the track and in the cauterized portion of the cavity, which exerts a favorable influence in bringing about limitation of the disease, or even in effecting a final cure. Through the opening made iodoform can be introduced into the cavity, which offers additional advantage in treating osseous foci successfully by this pressure. *To insure a successful issue, it is absolutely necessary to prevent infection with pus-microbes through the opening by making the operation under strict antiseptic precautions, and protecting the puncture with an efficient antiseptic absorbent dressing until it is completely closed by cicatrization and epidermization.* Ignipuncture is most useful in the treatment of accessible foci in the epiphyseal extremities of the long bones and during the early stages of tuberculosis of the wrist and tarsus. In incipient tuberculosis of the tarsus I have repeatedly obtained a satisfactory and permanent result by making an opening through the entire tarsus from side to side, in a line of the disease, by inserting the point from each side, the two tunnels meeting in the centre. Ignipuncture always relieves the pain promptly, and the track made is completely closed by permanent tissue in the course of a few weeks.

3. Radical Operation—(**a**) **Removal of Limited Foci.**—The radical treatment of tuberculosis of bone consists in the complete removal of the infected tissues by operative interference. The success which follows this treatment is most marked in cases where caseation has not taken place,—that is, in the granulating form,—and in other forms where the operation is performed before extensive secondary pathological conditions have occurred. The operation is indicated as soon as a positive diagnosis can be made, and after the milder measures have proved useless in arresting the progress of the disease. Timely surgical interference in osteo-tuberculosis is not only calculated to become the surest means of preventing general infection, but it also has for its object the limitation of the disease by the removal of the primary cause, and by accomplishing these objects it becomes at once a prophylactic as well as a curative measure. If a tubercular focus or foci can be removed by a radical operation before the adjacent joint has become infected, then the operation has not only been successful in effecting a permanent cure, but it has also been instrumental in preventing the extension of the disease to the joint. If the operation is undertaken at a time, as it should be, before any external swelling has appeared, the surgeon must be guided in finding the focus by searching for tender points, aided, if necessary, by exploratory punctures. As in epiphyseal tuberculosis the foci are always near a joint, the incision for exposing the bone should be made in such a manner as to avoid opening the joint. If the focus is so close to the joint as to make it necessary to remove bone underneath the insertion of the capsule or ligaments of the joint, it is advisable to lift the periosteum with the joint structures from the bone to some distance from the incision, and in this manner to avoid injury to the joint. The bone overlying a tubercular abscess is usually softened and easily removed with a small, round chisel. The limb should always be rendered bloodless by using Esmarch's constrictor, so that the operator can identify the tissues as they are being removed during the operation. If, after tunneling the bone for a considerable distance, the focus is not found, it is advisable to make from this track exploratory punctures in different directions with a small perforator until the cavity is found, which is then freely exposed with the chisel. As soon as this has been done the sharp spoon is used, with which the necrosed bone, granulation tissue, or cheesy material is removed. The osteoporotic bone in the immediate vicinity of the cavity is removed in a similar manner, and the surgeon must assure himself, by repeated examinations of the tissue removed, that healthy tissue has been reached before the sharp spoon is laid aside.

If any doubt remain whether all of the infected tissue has been removed, it is better to resort to ignipuncture, perforating the bone at different points to the depth of a few lines with the sharp point of a Paquelin cautery in addition to the curetting. This procedure will destroy at least some of the bacilli which might have remained, and will incite a plastic osteomyelitis that will effectually resist the pathogenic action of such microbes that still remain. After the cavity has been thoroughly irrigated with an antiseptic solution it is dried, iodoformized, and packed with antiseptic decalcified bone-chips. The periosteum is separately sutured over bone-packing, sufficient space being left to insert, at the low angle of the wound, a few threads of catgut to serve as a capillary drain. The remaining tissues are included in the superficial sutures and an antiseptic dressing applied. The limb must be immobilized by applying a well-padded posterior splint. If all the infected tissues have been removed, and no infection with pus-microbes has taken place during or after the operation, the wound unites under one dressing in from one to two weeks, and the definitive healing of the cavity is completed in the course of three to six weeks, according to the condition and age of the patient and the size of the cavity. The packing of such cavities with iodoformized decalcified bone-chips is an important element in the prevention of a local recurrence and general infection. Should suppuration follow the operation, secondary implantation with decalcified bone-chips can be done successfully as soon as suppuration has ceased, and the cavity can be made thoroughly aseptic.

(b) Excision of Portion of Shaft.—This operation is only indicated in some cases of diffuse tubercular osteomyelitis where amputation is considered unnecessary. Extirpation of the entire bone affected is frequently necessary in tuberculosis of the wrist and ankle-joint.

(c) **Amputation.**—Amputation is often the only choice in the treatment of diffuse tuberculous osteomyelitis, as it offers the only chance to effect complete eradication of the disease, and to protect the patient against general infection. It is contra-indicated in the other forms of osteo-tuberculosis, unless complicated by tuberculosis of an adjacent joint, and even in such instances it is limited to cases that have passed beyond the reach of a typical or atypical resection.

TUBERCULOSIS OF JOINTS.

Tuberculosis of joints, chronic fungous arthritis, strumous arthritis, and tumor albus are terms that even now are being used synonymously to indicate a form of inflammation of joints which clinically is characterized by its chronic course and the absence of acute signs of inflammation. This affection is by far the most common joint disease, so much so that König states that in surgical clinics the surgeon will have 100 cases of tuberculosis of the joints to deal with to one of the other classes of inflammation, such as gonorrhœal, syphilitic, suppurative, osteomyelitic, rheumatic, or the metastatic inflammations subsequent to acute infectious diseases.

Etiology.—We distinguish, as to origin, between primary synovial and primary osteal tuberculosis of the joints. If the primary focus is in the bone the disease usually extends to the joint by direct extension of the process to the structures of the joint. In primary synovial tuberculosis the bacillus is conveyed through the circulation, and localization takes place in the synovial membrane.

Max Schüller proved experimentally, in animals infected with tubercle bacilli,—for instance, through the respiratory tract,—that a slight traumatism to a joint would determine localization, by way of the circulation, to the injured part, and that a tubercular synovitis or panarthritis would follow. The same author makes the statement, based on the results of his experiments, that a slight injury to a joint in a person who has bacilli floating in his blood would determine localization, commonly in the form of a synovial tuberculosis. Clinically, tuberculosis of joints has been traced in 56 per cent. of the cases to traumatism by a direct blow to a joint, or distortion, or overexertion. It is characteristic that the traumatism is always slight; a severe injury, causing intra-articular fracture, is very rarely followed by tuberculosis, for the same reasons that severe injuries do not produce the disease in bone and other organs. It may be stated that, as to the relative frequency of the two forms of infection, it has been shown that primary osteal tuberculosis occurs two or three times as often as the primary synovial. Tuberculosis of joints is always closely related to the same disease in bone, because, when it does not follow the latter as a secondary lesion, the primary synovial not seldom implicates the adjacent bone from the direct extension of the infection from the fungous synovial membrane to the subjacent bone structure. Synovial tuberculosis is more frequent in the adult than in children. Primary infection of a joint is possible only through a wound, as in the case referred to under the head of Inoculation-Tuberculosis. Tubercular infection of an intact joint presupposes the entrance of the bacillus of tuberculosis through the respiratory tract or alimentary canal, or through some external infection-atrium into the systemic circulation, or the diffusion of bacilli through the same channel from some pre-existing tubercular focus, and the localization of floating bacilli in the synovial membrane by capillary embolism or by mural implantation. A simple tubercular nodule over the surface of the synovial membrane may lead, in a comparatively short time, to diffuse tuberculosis over the entire surface of the joint by local dissemination of the microbes, in which the synovial fluid and the movements of the joint play an important part. In the osteal form of tuberculosis of joints the infection extends from the bone to the joint at once, in cases where the primary disease is the result of infarction, as the base of the wedge-shaped piece of the necrosed bone communicates directly with the joint; while infection of the joint occurs secondarily, in cases of granulating foci and tubercular necrosis, by perforation of the tubercular product into the joint. When the foci are located close to the articular cartilage, this must be destroyed before the joint is invaded, the cartilage forming a barrier that may sometimes prove sufficient to resist invasion. In case a focus is located at the surface of a joint, where the bone is not covered with articular cartilage, the thin periosteum and the synovial membrane covering it are more easily perforated, and consequently secondary synovial tuberculosis is more liable to follow. The most complicating condition may arise if a tubercular focus is located at the insertion of the capsule of a joint. It may then open into and outside of the joint simultaneously, or the one or the other, the integrity of the joint depending on the few lines of space occupied by the capsule.

Pathology and Morbid Anatomy.—In synovial tuberculosis a series of pathological changes are initiated in which all the structures of the joint are finally concerned, namely, the synovial membrane, para-synovial tissues, articular cartilage, and lastly the bone. The tubercle-nodule in the synovial membrane presents, under the microscope, the same histological structure as in other tissues. When the synovial surface has become the seat of diffuse tuberculosis, the tissues undergo the same pathological changes as during the first stage of tuberculosis in other organs, and it is the characteristic granulation tissue that has given to this form of arthritis the names of *fungous synovitis* and *synovitis hyperplastica granulosa.* During the early stages of the disease the surgeon meets with two distinct varieties; in one the tubercular infection produces a pulpy condition of the entire synovial sac, with little or no effusion into the joint, the swelling being due entirely to the presence of a thick layer of granulation tissue,—the true *tumor albus* of the old writers. This form of tuberculosis gives rise, at an early stage, to extensive deformity of the joint, flexion, rotation, and, in the case of the knee-joint, partial dislocation of the tibia backward. In the other variety the fungous granulations are less marked, but a copious effusion takes place into the joint, which simulates a catarrhal synovitis, until time and the effect of treatment enable the surgeon to make a correct differential diagnosis. In this form König assures us that he has never observed a tendency to flexion or any other form of displacement of the joint surfaces. If suppuration take place, which is not very often the case, it begins in the granulations which cover the synovial membrane, and the pus accumulates in the cavity of the joint until perforation of the capsule takes place. During the suppurative process the granulations are destroyed and the tubercular infection penetrates deeper, and, as during the destructive process blood-vessels are destroyed, the patient is exposed to the additional risks of general infection. If a tubercular joint open spontaneously, or is not incised under the strictest antiseptic precautions, the additional infection from without leads to the most serious consequences, as under these circumstances the pus-microbes are brought in contact with a surface that has been admirably prepared by the bacillus of tuberculosis for suppurative and septic processes.

Pathological Varieties of Joint Tuberculosis.—Tubercular inflammation of the synovial membrane of joints results in different gross pathological conditions that serve as a basis for classification into: 1. Pannous hyperplastic synovitis. 2. Tuberous hyperplastic synovitis or papillomatous plastic synovitis. 3. Granular or fungous hyperplastic synovitis. 4. Tubercular articular empyema.

1. Pannous Hyperplastic Synovitis.—The tubercle-nodules are extremely small, rarely visible to the naked eye, and widely disseminated over the entire or greater portion of the synovial sac. The synovial membrane is only moderately thickened, but quite vascular. From the border of the cartilage a thin, vascular layer of granulations approaches the centre of the surface of the joint somewhat in the manner a pannus invades the cornea. This form of synovitis was first des

2. Tubercular Plastic Synovitis or Papillomatous Plastic Synovitis.—The tubercular inflammation results in the formation of sub-synovial fibrous masses, which may attain the size of a walnut, protruding into the joint and filling, for example, the supra-patellar recess of the knee-joint, with simple irritative synovitis or pannous synovitis in the rest of the cavity. The tubercular infection in such cases is limited, and the removal of the fibrous swelling results in a permanent cure. In other cases of the same type of inflammation the foci are numerous, resulting in papillomatous plastic synovitis where the whole inner surface of the synovial membrane is covered with sessile or pedunculated papillomatous growths, small and rather uniform in size, some of which may become detached, when they constitute the so-called rice-bodies.

3. Granular Fungous Hyperplastic Synovitis.—In this variety of joint tuberculosis the synovial membrane is affected throughout, being considerably thickened and hyperæmic, and covered by a more or less thick layer of velvety granulations. The ligaments and para-articular structures are affected at a comparatively early stage, and thus is formed the thick, œdematous mass of tissue, usually of a gelatinous appearance, in which here and there cheesy foci are found.

Any of the above-named forms of tubercular synovitis may give rise to the transudation of serum or a sero-fibrinous fluid into the joint,—the tubercular hydrops of König. As a rule, the serous effusion is most copious in cases where the synovial membrane has undergone the least change; that is, in pannous hyperplastic synovitis. In tuberous and papillomatous synovitis the effusion is usually scanty, and in fungous synovitis attended by the formation of massive granulations it is absent, as a rule. The effusion into the joint, in tubercular hydrops, is either a thin, clear synovia, or it is rendered slightly turbid from the admixture of leucocytes and the products of coagulation necrosis, or, if the effusion is of a sero-fibrinous character, it contains shreds of fibrin. The rice-bodies (*corpora amylaceæ*), so frequently found in tubercular joints, are composed of dense masses of fibrin or they are detached papillomata. That these bodies are a tubercular product I have repeatedly satisfied myself by inoculation experiments.

4. Tubercular Articular Empyema (*König*).—The tubercular abscess of joints is an advanced stage of the other varieties of tubercular synovitis. The inside of the capsule is covered with loosely-adherent tuberculous membrane, similar to that in tubercular abscesses. The superficial granulations which compose this membrane have undergone degenerative changes. Outside of this membrane the tissues are diffusely infiltrated with miliary tubercles, but the infection does not extend beyond the synovial membrane. The fluid in the joint, like in all tubercular abscesses, is not pus, but serum, in which we find suspended the products of coagulation necrosis. With the extension of the tubercular process beyond the limits of the synovial sac, the articular cartilage, and, finally, the bone, are successively attacked. The articular cartilage takes no active part in the inflammatory process; it is detached and removed by the granulations. An osseous focus in contact with the cartilage usually makes a circular defect through which the granulations or cheesy material can be seen. The cartilage covering a tubercular infarct is rapidly destroyed, and is mechanically detached in smaller or larger fragments. In primary tuberculosis of the synovial membrane the process usually commences at the periphery of the articular cartilage, and from here the granulations dip down into the vascular bone, and often undermine the cartilage extensively before any destructive changes are witnessed on the side directed toward the joint. In such cases the cartilage is not only often extensively detached, but perforated at numerous points by the granulations underneath it. The action of the granulations on the articular extremities of the bone produces a condition which has been described for centuries as caries. *Caries* is not a disease, but the result of a disease. The bone becomes softened, and by molecular disintegration, caused by action of the granulations, it becomes porous and honey-combed. Numerous miliary nodules can be seen in the affected area, which, in the course of time, undergo coagulation necrosis and caseation. In long-standing cases the destruction of bone is so extensive that in the hip-joint, for instance, it may result in the loss of the entire head of the femur and perforation of the acetabulum.

Symptoms and Diagnosis.—The symptoms vary according to the type of the disease and manner of infection. With the exception of circumscribed points of tenderness outside of the region of the joint that indicate the existence of primary osteo-tuberculosis, we have no symptoms which enable us to make a positive diagnosis between a primary osteal and a primary synovial tuberculosis of a joint. The primary osteal form is the most common. In the knee the proportion of the primary osteal to the primary synovial form is in the proportion of 3 to 1; in the hip, 4 to 1; in the elbow, 4 to 1. As to age, the proportion is, in children below 15 years of age, 2 to 1; above 15, 3 to 1. In reference to the location of the joints affected, it can be said that joint tuberculosis is much more frequent in the lower than in the upper extremities. According to Albrecht, out of 325 cases, in 91 the disease affected the joints of the upper, and in 234 those of the lower, extremities.

1. Swelling.—In the atrophic form of plastic synovitis, the *caries sicca* of Volkmann, so common in the shoulder-joint, there is not only no swelling, but the region of the joint may even be found atrophied from muscular atrophy. The absence of swelling and the presence of considerable mobility in the joint may lead to a wrong diagnosis under the impression that the affection is a neurosis. A careful examination under the influence of an anæsthetic will, however, reveal restriction of mobility from cicatricial contraction of the tubercular capsule, which will enable the surgeon to make an early and correct diagnosis. The swelling resulting from tubercular hydrops and abscess is caused exclusively by distention of the capsule with fluid, as the capsule in either case is but little thickened and the granulations are scanty. In both of these conditions the capsule of the joint is often enormously distended. In the knee-joint the patella is raised from the condyles of the femur, and the depression on each side of it, present in a normal condition in the extended position of the limb, is not only effaced, but replaced by a well-marked prominence. Fluctuation is distinct. In the dry, fungous variety of synovitis the swelling is due to the masses of granulation tissue within, and, after perforation of the capsule has occurred, within and outside of the joint. This is the most common of all the forms of articular tuberculosis. The old authors were of the opinion that the œdema in the neighborhood of a white swelling was due to expansion or enlargement of the articular extremities of the bones, until Samuel Cooper pointed out that it was caused by thickening of the capsule. The granulation tissue is often present in such abundance as to give rise to considerable distention of the joint, and, in the knee-joint, elevating the patella from the condyles of the femur to such an extent that the contour of the joint simulates an effusion into that articulation. The granulations are so soft that on palpation in these cases fluctuation can be distinctly felt, especially if the capsule of the joint is very thin from overdistention or destructive changes. To ascertain the character of the contents of such a joint, it is usually necessary to resort to an exploratory puncture. The invasion of the para-articular tissues causes considerable swelling in the region of the joint, imparting to the latter the characteristic spindle shape so frequently found in the knee-, elbow-, and ankle- joint, the swelling being so much the more conspicuous when atrophy of the muscles above and below has taken place. Extension of the infiltration from the para-articular tissues in the direction of the subcutaneous tissues finally causes the swollen joint to be covered with a whitish, immovable, dense skin, giving the joint the appearance from which the time-honored name of *white swelling* was derived. If a peri-articular abscess appear the swelling of the joint is generally diminished, while a new swelling forms in the vicinity or some distance from the joint.

2. Pain.—Pain, as a symptom accompanying tuberculosis of joints, although always present, is of extremely variable intensity. In some cases it is so slight that patients will continue to use joints distended with masses of fungous granulations without much suffering, while in other instances a limited disease in the joint will cause complete disability and a great deal of suffering. According to my observation, the pain is usually more severe in cases where the granulations are scanty than when the synovial membrane is the seat of extensive fungosities. As a point in differential diagnosis, it may be said that in osteal tuberculosis pain is present from the beginning in the bone, and is not much aggravated by the joint disease; while an almost painless primary synovial tuberculosis is attended by severe pain, with nocturnal exacerbations as soon as the synovial membrane and articular cartilages have been destroyed and the bone has been secondarily implicated in the inflammatory process. Absence of tenderness away from the joint and its presence in the line of the joint would indicate rather a primary tuberculosis than the osteal variety. In primary synovial tuberculosis in the hip-joint the pain is located in the joint and the groin; while in the osteal form, during the early stage at least, it is usually referred to the inner aspect of the knee.

3. Deformity.—Contraction, lateral deviations, subluxations, and other abnormal positions usually indicate more or less destruction of the articular surfaces of the bones and lateral ligaments. These malpositions are not seen in articular tubercular hydrops or the milder forms of synovial tuberculosis, while we find different degrees of one or more of them nearly in every case of advanced fungous synovitis. In advanced cases of synovial tuberculosis of the knee-joint the joint is flexed, the leg rotated outward, and the head of the tibia displaced backward. In the hip-joint the disease gives rise to flexion of the thigh upon the pelvis, and first eversion, but later inversion, of the limb. After separation of the head of the femur, or extensive destruction of the articular end of this bone and the acetabulum, the contour of the region of the hip-joint and the position of the limb simulate dislocation of the head of the femur upon the dorsum of the ileum. Tubercular disease of the elbow-joint gives rise to flexion and pronation of the forearm. The clinical importance of any of these displacements lies in the fact that they signify a certain amount of destruction of the joint structures, thus often indicating surgical interference for the correction of the deformity, as well as the removal of the diseased tissue. Remembering the frequency of tubercular affections of joints, as a rule, there is little difficulty in their recognition, if the history, course, and symptoms are carefully studied and analyzed. König justly remarks that it is well to remember that articular tuberculosis, even if the disease affect a large joint, is practically a local disease, and has for a long time little or no influence on the general health of the patient. Thus, we may find patients presenting all the appearances of robust health suffering from articular tuberculosis. The tubercular articular hydrops is distinguished from a catarrhal or rheumatic synovitis with copious effusion by its persistency and tendency to return after aspiration or after active use of the joint. The presence of flocculi or rice-bodies in a joint confirm the tubercular nature of the affection. A tuberous synovitis, with the formation of a single mass of fibrous tissue, sessile or pedunculated, might be mistaken for lipoma arborescens or gummata. The diagnosis of the latter will be cleared up by a course of antisyphilitic treatment, which should always be instituted in cases of doubt. Tubercular joint abscess is distinguished from suppurative, gonorrhœal, or rheumatic synovitis by the pain being less and the absence of all signs of acute inflammation. The local conditions in fungous synovitis are so characteristic that they can hardly be misinterpreted by a careful observer. The presence or absence of fluid in the joint has often to be determined by an exploratory puncture. The *caries sicca* of Volkmann, or dry, pannous, hyperplastic synovitis of Hueter, especially as found in the shoulder-joint, might be mistaken for a neurosis, with atrophy of the muscles covering the joint. The differential diagnosis can be made by making the examination while the patient is fully under the influence of an anæsthetic. If the affection is a neurosis, motion will be found unimpaired; if it is tubercular, the mobility of the joint will be found lessened by intra-articular adhesions and cicatricial contraction of the capsule of the joint.

Prognosis.—Tuberculosis of a joint may terminate in a spontaneous cure in cases in which the intensity of the infection is slight, or the resistance on the part of the patient is so great that the fungous granulations do not undergo degenerative changes, but are converted into connective tissue. A partial or complete synechia of the cavity of a joint is often one of the unavoidable results in such cases, leaving the joint in a permanently stiff condition. This endeavor on the part of the organism to limit the extension of the disease is often observed in cases in which the joint affection occurs in connection with osteal tuberculosis. As soon as perforation of a focus into a joint has occurred a wall of granulation tissue is thrown out around the circumscribed area of infection, and, under favorable circumstances, a partition of cicatricial tissue is formed which isolates the infected from the intact portion of the joint. In such instances we have an illustration how the tubercular process is retarded, and sometimes permanently arrested, by the transformation of granulation into connective tissue. For such a favorable termination to take place it is necessary that the tubercular virus should be attenuated by age or want of a proper nutrient medium, or that the pathogenic effect of the bacilli should be neutralized by an adequate resistance on the part of the tissues before degenerative changes have occurred in the granulation tissue. The course of articular tuberculosis is so variable in different cases that it is impossible, during the early stages of an attack, to predict anything certain in reference to the probable outcome. A spontaneous cure is more likely to take place if the patient is young, not anæmic, and, at the same time, well nourished. The hygienic surroundings must also be taken into consideration in rendering a prognosis. The disease shows greater tendencies to limitation in children than in persons past the age of puberty.

Among the different forms of joint tuberculosis the tubercular hydrops and caries sicca are the most benign, and in these cases a spontaneous cure is most frequently realized and the same conditions are effected, and which are also amenable to successful surgical treatment. The caries sicca may, according to König, terminate in a spontaneous cure in two or three years, with some loss of motion in the joint. It is sometimes difficult to ascertain in a given case when the lesion can be considered as cured. As the most reliable evidences that such favorable termination has taken place must be considered disappearance of swelling, pain, tenderness, and restoration of function as far as this can be expected. The patient should not be permitted to use the limb until the active symptoms of inflammation have disappeared. The danger to life arises from the existence of complications, foremost among them being septic infection, pulmonary or general tuberculosis, and amyloid degeneration of important internal organs. Septic infection is caused either by localization of pus-microbes brought to the tubercular focus through the circulating blood, or, what is more frequently the case, through an infection-atrium, created by a spontaneous opening through an operation wound, or, finally, through a fistulous communication with the joint. Many neglected cases of joint tuberculosis die annually of pulmonary or general tuberculosis. Billroth states that in sixteen years 27 per cent. of bone and joint tuberculosis were lost in this way. König, from a table of 117 operations for tuberculosis, found that after four years 16 per cent. had died from general tuberculosis. If a patient escape death from septic infection, after secondary infection with pus-microbes, he is liable to succumb several years later to amyloid degeneration of the spleen, the liver, and especially the kidneys, with its accompanying anasarca.

Treatment.—As spontaneous cure in cases of joint tuberculosis is more frequently the exception than the rule, and if finally it does take place it does so generally after the limb has become so much deformed that it has become useless and will require a formidable operation to restore partial function, it is evident that timely surgical treatment should be adopted to eradicate the disease, preserve function, and, at the same time, protect the patient as far as can be done against general infection.

I. Rest.—As in cases of osteo-tuberculosis, rest is an important element in the treatment of tubercular joints. It is even more important to secure rest for an inflamed joint than for an inflamed bone, as the inflammation is always greatly aggravated by the movements in the joint that necessarily take place as long as the joint is used, which does not apply with equal force to cases of osteo-tuberculosis. The best method to fulfill this indication is to immobilize the limb in a plaster-of-Paris splint, which does not necessarily confine the patient to his room or bed. If one of the lower extremities is to be encased in a plaster splint, I am in the habit of applying the plaster-of-Paris roller over tight-fitting knit drawers, which protect the skin much better than an ordinary roller bandage. All bony prominences should be protected against pressure by careful padding with absorbent cotton. If the hip-joint is the seat of inflammation the splint is applied with the limb in the extended position, while the patient stands on the sound limb upon a low stool, as in this position autoextension is made by the weight of the suspended limb. In such cases the splint must extend from the toes and embrace the entire limb, the whole pelvis, and abdomen as far as the umbilicus, and the opposite limb as far as the knee-joint. In tuberculosis of the knee-joint the splint should extend from the toes to the groin, and, in ankle-joint affections, from the toes to the knee-joint. Immobilization is to be made with the limb in such a position that in case the joint should become permanently stiff the limb can be used to greatest advantage. A slight degree of flexion in the hip- and knee- joint is to be preferred to a perfectly straight position. In inflammation of the shoulder-joint the limb makes the necessary counter extension and fixation of the joint by confining the limb, with the forearm flexed, at right angles to the side of the chest, by strips of adhesive plaster or a plaster-of-Paris bandage. The hand should be slightly extended in immobilizing the forearm in the treatment of tuberculosis of the wrist, while the forearm is flexed at a right angle to the arm in tubercular synovitis of the elbow-joint, with the hand in position half-way between pronation and supination. Early immobilization of a tubercular joint not only secures absolute rest for the joint, but, at the same time, this treatment prevents to a great extent subsequent deformities. Treatment by immobilization should be continued until all symptoms of inflammation have subsided, or until more radical measures become necessary. If the arthritis has already resulted in contractures the treatment by extension with weight and pulley is in place, and should be continued until the limb has been brought in proper position for treatment by immobilization.

2. Aspiration.—In tubercular hydrops the intra-articular effusion is often very copious, resulting in enormous distention of the capsule of the joint, which, if continued for any length of time, must necessarily result in great weakening of the joint. Aspiration under these circumstances relieves the distention and places the vessels in the synovial membrane in a better condition to perform their function in the subsequent removal of the inflammatory product by absorption. After evacuation of the contents of the joint the limb should be immobilized and rapid re-accumulation of the fluid prevented by uniform, equable compression of the joint by strips of adhesive plaster or rubber bandage.

3. Subcutaneous Evacuation of Contents of Joint, followed by Iodoformization.—In tubercular hydrops and abscess of a joint, subcutaneous evacuation of the fluid contents, followed by iodoformization practiced in the same manner as has been described in the treatment of tubercular abscess, yields much more satisfactory results than simple aspiration. In tubercular hydrops irrigation of the joint with a 3-per-cent. solution of boric acid is only necessary for the removal of rice-bodies; if such are not present, the iodoform mixture may be injected at once. Tubercular abscess always requires a preliminary irrigation with some mild antiseptic solution, for the purpose of removing detached and disintegrated tubercular products before the iodoform mixture is injected. Krause, in the last eighteen months, treated 43 tubercular joints by means of iodoform injections; cases were treated by other means, and where cure without operation seemed impossible, but in which fistulæ were not yet formed. The injections were repeated at intervals of two or three weeks. Pain was greatly relieved by this treatment; the swelling yielded much more slowly, though in six weeks some cases showed a reduction in size and a hardness of the affected parts. The abscess-cavities frequently filled again, rapidly at first, but ultimately re-accumulation ceased. In some cases fistulæ formed at the seat of puncture, which first discharged pus, then serum, but ultimately healed entirely. In a fair percentage treated in this way definitive healing was obtained. This treatment promises the best results in cases where granulation tissue is scanty, and where the inflammatory product has not undergone extensive caseation. Its utility is much impaired if suppuration has taken place in the joint. Billroth opens the joint, evacuates its contents through the incision, removes (if present) tubercular sequestra, rice-bodies, and tubercular membranes, and then treats the joint by iodoformization. In general practice, however, it is much safer to follow the subcutaneous method by puncturing the joint with a medium-sized trocar, using the canula for evacuation, irrigation, and iodoformization.

4. Arthrectomy.—Excision of the infected tissues in primary tuberculosis of the synovial membrane has been practiced for a number of years, and the results of this treatment have been quite encouraging. Primary synovial tuberculosis, without any foci in the articular ends of the bones, should be treated by arthrectomy and not by resection, as by the former operation the diseased tissues can be removed effectually without unnecessary loss of healthy tissues that are sacrificed by the latter operation. The success of an operation for tubercular affections depends largely upon the thoroughness with which the operation is done and the absence of suppuration. Arthrectomy should be performed before fistulous openings have formed, and the joint must be opened by an incision that will expose every nook and corner of the capsule. Of the many incisions that have been devised for opening the knee-joint, the one I shall describe here offers the greatest advantages and is open to the least objections. The old-fashioned horseshoe incision, with the convexity directed downward, makes it very difficult to suture the wound, and leaves a scar where it is most exposed to injury. The incision carried directly across the knee-joint, if the patella is divided at the same time, leaves, subsequently, the superficial and deep parts of the wound directly opposite; if the patella is preserved, the scar of the external incision falls upon the most prominent part of the patella, which is again a great disadvantage. The incision, which for several years I have always selected in opening the knee-joint in performing arthrectomy or resection, is slightly curved, but with the convexity directed *upward.* It is carried from the most dependent portion of the knee-joint, at a point corresponding to the most prominent part of the internal condyle of the femur, in a gentle curve to the upper border of the patella, and from here downward and outward to a point opposite where it was commenced. The short, semilunar, cutaneous flap is now detached and turned downward. After this an incision is carried directly across the joint, dividing the lateral ligaments and crossing the patella transversely at its centre. The patella, at this step of the operation, is divided with a saw. The upper recesses of the synovial sac are freely opened by making an incision on each side of the upper half of the patella, which is carried as far as the upper recess of the synovial sac. The rectangular flap, composed of the upper end of the patella with its muscular attachments, is reflected, which exposes every portion of the upper part of the synovial recess. A somewhat similar flap is made of the lower half of the patella and its tendon, reflected in a downward direction, by which the tissues underneath that portion of the patella and its ligament are fully exposed. With the knee-joint thus exposed it is not difficult to extirpate, with the help of a catch-forceps, a sharp scalpel, and a pair of curved scissors, the entire capsule. The part of the capsule that will be found most difficult to remove is that portion which covers the popliteal vessels, and dips down behind the condyles of the femur and behind the tuberosities of the tibia. During this part of the operation the leg must be forcibly flexed over a small cushion, or the fist of an assistant, in the popliteal space. Arthrectomy is always a tedious operation, as it is absolutely necessary to remove all of the infected tissues in order to secure permanent success. If the patella is not diseased it should never be removed. After the capsule has been extirpated the patella is united by two chromicized catgut sutures. I have never failed in obtaining bony union in four to six weeks after this method of coaptation. After extirpation of the capsule, and before the elastic constrictor is removed, the whole surface should be once more irrigated with a hot solution of corrosive sublimate (1 to 1000), after which it is rubbed off with dry iodoform gauze, in order to remove any detached fragments that have not been washed away. The whole surface is now freely sprinkled with impalpable iodoform, which is rubbed into the surface. Before the constrictor is removed the wound is packed with aseptic gauze, the flaps are laid over it, and manual compression made for five to ten minutes after the removal of the constrictor, with the limb in an elevated position. This simple procedure serves an admirable purpose in controlling capillary hæmorrhage, and reduces the necessity of recourse to ligature to a minimum.

After all the bleeding has been arrested, the patella is sutured, and the deep parts of the wound are united by buried sutures. Tubular drainage can usually be dispensed with, as a capillary drain composed of a few threads of catgut will answer an excellent purpose, and will not, like the tubular drain, necessitate an early change of dressing. The external incision is closed with silk sutures, the line of suturing being out of the way of the patella, the parts united with the buried sutures being covered throughout by the external flap. A careful hæmostasis and rigid antiseptic precautions will make it unnecessary to change the dressing earlier than the end of the second week, and on this account I prefer to immobilize the limb in a plaster-of-Paris splint applied over a copious antiseptic dressing. The limb must be kept in an elevated position for at least six hours after the operation, so as to diminish the amount of parenchymatous hæmorrhage. If all the infected tissues have been removed and the wound remains in an aseptic condition, the external wound will be found closed in the course of two or three weeks. A fair restoration of function with partial mobility of the joint can be expected in favorable cases. Passive motion must be delayed until the patella has firmly united, which will require from three to four weeks in children and nearly twice this length of time in adults. After the patella has united and the external wound is completely healed, recovery is hastened by passive motion, massage, and use of the faradic current. Arthrectomy has a future in the treatment of primary synovial tuberculosis of the knee-joint, but for well-known anatomical reasons it is not equally applicable in the treatment of synovial tuberculosis of any other of the larger joints. It is possible that the operation will be modified and sufficiently perfected in the future so as to be applicable in the treatment of synovial tuberculosis of the hip- and shoulder- joint. In 2 cases of tuberculosis of the elbow-joint I obtained an excellent result from arthrectomy combined with temporary resection of the olecranon process. This process was divided obliquely with a saw at its junction with the shaft of the ulna, and, after the extirpation of all of the infected soft tissues of the joint, the process was fastened in its proper place with an aseptic ivory nail. The functional result was satisfactory.

5. Atypical Resection.—The incision in atypical and typical resection of the knee-joint should be the same as has been described above. The patella is divided transversely, and, if it does not contain a tubercular focus, it is not necessary or advisable to remove it, as its continuity, after resection, can be restored by suturing with a durable form of catgut. An atypical resection consists in the removal of tubercular foci in the epiphyseal extremities of the bones that enter into the formation of the joint, without removing the entire articular extremities by a transverse section with the saw. The unnecessary removal of the epiphyseal extremities should especially be avoided in the case of children, as the removal of one or both centres of growth of bone will result in so much shortening of the limb subsequently as often to render it not only perfectly useless, but it becomes a burdensome appendage. In children atypical resection should be practiced in all cases where all the foci in the articular extremities can be reached and removed by this method. The proper instruments to be used in this operation are the chisel, bone-forceps, and sharp spoon. After the joint has been freely opened, the articular surfaces are carefully inspected for evidences of deeply-seated foci. If perforation into the joint has taken place, the cavity is freely exposed from the articular surface, and all of the infected tissues are removed with chisel and sharp spoon. It is important not only to remove necrosed bone, granulation tissue, and caseous material, but also the surrounding osteoporotic zone of bone that possibly might contain tubercle bacilli. A deep-seated focus may be suspected and searched for if the articular cartilage has become detached over a greater or less extent. Explorations with a small perforator can be made in different directions from the articular surface in searching for deeply-seated foci. If the articular cartilage has become detached over a considerable area by granulations underneath it, it should be removed, and the exposed bone must be subjected to another careful examination for the purpose of locating and treating deeply-seated foci. A circumscribed area of great vascularity is a suspicious indication, and calls for a limited excavation with a small, sharp spoon for diagnostic purposes. It is well for the surgeon to remember that primary osteo-tuberculosis with secondary involvement of a joint usually consists of more than one focus in one or both epiphyseal extremities. A tubercular infarct is generally recognized by examining the articular surface, as the cartilage or the exposed portion of the wedge-shaped sequestrum presents appearances of necrosis that cannot be mistaken. After the extraction of the sequestrum the tubercular cavity is submitted to the same treatment as when dealing with a granulating or caseous focus. In primary synovial tuberculosis, with extension of the disease to the subjacent bone, it becomes necessary to remove the honey-combed, softened bone over the entire surface with the sharp spoon and chisel. Before the operation is extended to the bone in osteo-tuberculosis, it is always necessary first to extirpate with knife and scissors the infected soft structures of the joint, the synovial membrane and ligaments, as otherwise the healthy vascular bone may become an infection-atrium for traumatic infection,—a not very infrequent and serious complication after operations on bones and joints for tuberculous affections.

Wartmann, after giving a careful account of the results following excision of tubercular joints in the hospital practice of Feurer, gives the statistics of 837 cases of excision of joints for tuberculosis from the practice of different operators. Of this number 225 died. Of the fatal cases, in 26 death followed the operations closely, and resulted from acute tuberculosis, probably induced by the operation. König observed 16 cases in his own practice in which miliary tuberculosis followed almost immediately after operations on bones and joints for tubercular affections. König states that the secondary infection sets in seven to ten days after operation, which may have been perfectly aseptic, with healing of the wound by primary union. The secondary tubercular infection appears either as an acute pulmonary tuberculosis or tubercular meningitis, terminating in death three or four weeks after the operation. It is not difficult to conceive the *modus operandi* of such an occurrence. The resection wound opens numerous veins in the bone, the lumina of which remain patent, ready for the introduction of minute fragments of granulation tissue or bacilli, which, on entering the venous circulation, are the direct cause of metastatic tuberculosis in distant organs. We must take it for granted in such cases that a tubercular focus, during the operation, furnished the essential infected fragments of granulation tissue, or free bacilli are aspirated or forced into the openings of wounded vessels, and through them gain entrance into the general circulation. To guard against such an accident, it is necessary to remove from the joint all possible source of infection before operating on the articular extremities. Cartilage that remains firmly attached to the bone may be left. After all foci have been radically eliminated, the field of operation is flushed with an antiseptic solution, and, after drying and iodoformization, the bone-cavities are packed with decalcified antiseptic bone-chips, and the operation is completed in the same manner as in arthrectomy.

The treatment of bone-cavities with decalcified bone-packing is of the greatest utility in atypical resection. An atypical resection with subsequent implantation of decalcified bone has for its objects complete removal of the infected tissues in the joint and the surrounding bone, and the partial restoration of the parts destroyed by disease or removed during the operation. In atypical resection of the knee-joint it is not uncommon that nearly an entire condyle of the femur or tuberosity of the tibia must be removed. In such cases the surgeon aims at bony union between the articular ends of the bones, which is accomplished in the most satisfactory manner by placing the parts in a condition to repair the lost bone-tissue, which may be done by filling the defect with decalcified bone-chips. I have repeatedly made excavations in one of the condyles of the femur and in the head of the tibia from the joint surface, the size of a small orange, and obtained bony ankylosis, with the limb in a good position, by filling the cavities with bone-chips. As the bone-chips are always iodoformized before implantation, they serve a useful purpose not only by furnishing a temporary scaffolding for the reparative material, but they constitute a valuable therapeutic measure in the prevention of a local recurrence of the disease in case tubercle bacilli should remain in the cavity or its immediate vicinity. Immobilization of the limb after resection should be continued until the process of repair has been completed, which, under the most favorable conditions, requires from six weeks to two months. Atypical resections are applicable only to certain joints, as the knee-, elbow-, ankle-, and tarsal joint. The elbow-joint is most accessible through a long, straight incision, and after temporary resection of the olecranon process. Atypical resection of the ankle-joint can be done through two lateral incisions, with chisel and sharp spoon. In all resections, atypical and typical, ignipuncture is indicated after the excision has been completed, if any portion of the bone is abnormally osteoporotic, as this procedure will stimulate the process of repair, and may prove useful in destroying infected tissues, which, from their macroscopical appearance, indicate a healthy condition.

6. Typical Resection.—In typical resection one or both articular extremities are sawn across and removed. In the hip-joint it implies the excision of the head, neck, and part or the whole of the greater trochanter of the femur. A typical resection of the wrist-joint means the removal of the entire carpus, with or without the articular surfaces of the radius, ulna, and metacarpal bones. In a typical resection of the shoulder-joint the head of the humerus is removed. In the knee-joint the operation means excision of the articular surfaces of the femur and tibia; in the elbow-joint, of the humerus, radius, and ulna; in the ankle, of the tibia, fibula, and astragalus. Typical resections are always made for tubercular affections of the shoulder-, hip-, and wrist-joint. In the remaining larger joints it is more frequently resorted to in adults than children. In children the operation is limited, with the exception of the shoulder-, hip-, and wrist-joint, to cases where the articular extremities are so extensively diseased that an atypical resection would fail in removing all of the infected tissues. Removal of the diseased synovial membrane and ligaments should precede section of the bones with the saw wherever, from the anatomical construction of the joint, this can be done. In the hip- and shoulder-joint the head of the bone must be removed first before the soft structures of the joint can be removed. The operation best adapted for resection of the hip-joint is the one devised by König, by which the borders of the trochanter major are preserved. In this operation the section of the bone must be made with a chisel. The entire neck and head of the femur are removed by dividing the bone transversely with a chisel just below the neck, with the exception of the borders of the greater trochanter, which are split off with the same instrument. The capsular ligament is removed as thoroughly as possible, and the acetabulum is scraped out with a sharp spoon. Provision for drainage must be made in all hip-joint resections. The after-treatment consists of rest in bed upon a smooth mattress, with the limb extended by weight and pulley in an *abducted* position. After six weeks the patient is allowed to walk on crutches, with a raised sole under the shoe, worn on the opposite side, so that the limb on the resected side makes the necessary autoextension. During the night extension is applied for eight months or a year, in order to prevent unnecessary shortening. Eversion and inversion of the limb while the patient is in bed are prevented either by a Volkmann railway-splint or by supporting the limb with sand-bags, applied to each side. Immobilization, after resection of the shoulder-, elbow-, wrist-, knee-, and ankle-joint, is best secured in a plaster-of-Paris dressing, which also serves an excellent purpose in keeping the antiseptic dressing *in situ*.

Temporary resection of the olecranon process in resection of the elbow-joint has yielded excellent results in my hands, as by it the insertion of the biceps muscle is not disturbed. The resected olecranon, after the removal of any foci it may contain, is riveted to a denuded surface of the shaft of the ulna with a sterilized ivory or bone nail after the resection has been completed. The forearm is immobilized in a semi-flexed position until bone union between the ulna and olecranon process has taken place, which usually requires about six weeks. After this time passive motion and massage should be made to increase the mobility of the joint. A straight, single incision upon the dorsal side is best adapted for resection of the wrist-joint, as the extensor tendons of the hand and fingers can be drawn aside sufficiently to afford ample room for the removal of the entire carpus. In the after-treatment of excision of the wrist the forearm and hand as far as the metacarpo-phalangeal joints are encased in a plaster-of-Paris splint, with the hand in a slightly-extended position. Immediate fixation of the resected ends by means of bone or ivory nails, after excision of the knee, is superfluous, as the parts can be kept in accurate position by ordinary fixation dressing. In knee-joint resections the section through the bones must be made in such a manner that when the sawn surfaces are brought in apposition the leg will be slightly flexed, as this position enables the patient to walk more gracefully than with a straight, stiff limb. The artificial support must not be removed until firm bony union has taken place, which will require from two to three months, according to patient's general health and age.

7. Amputation.—Amputation must be reserved for cases presenting special indications. It is the only operation that promises any benefit if the patient suffer from tuberculosis of other organs, provided the general conditions furnish no positive indications. It is also indicated if a tubercular abscess has perforated the capsule of a joint and has extensively infiltrated the surrounding tissues. This condition is to be expected if the limb has become œdematous some distance from the joint. The flaps must be taken from the side of the limb where the skin is in the best condition, and the incision through the deeper tissues must be made through healthy tissue. It is astonishing how rapidly wounds heal, and how quickly patients will recover after amputations for extensive local tubercular processes, even in patients greatly emaciated by the disease.

CHAPTER XXI.

TUBERCULOSIS OF TENDON-SHEATHS, ETC.

TUBERCULAR TENDO-VAGINITIS.

TUBERCULOSIS of the tendon-sheaths, or, as Hueter termed this affection, *tendo-vaginitis granulosa*, has only been recently recognized and described as a primary local tuberculosis.

Pathology.—Hueter was of the opinion that this affection is seldom met with as a primary lesion, but that it appears usually as a complication of joint tuberculosis. As a secondary lesion it is a frequent concomitant of osteal and synovial tuberculosis by direct extension of the inflammation from the primary focus to tendon-sheaths. Volkmann gave an able and accurate description of tendon-sheath tuberculosis in 1875, but at that time he was not aware of its tubercular nature. The first scientific treatise on this affection came from the clinic at Göttingen by Riedel, who showed that the rice-bodies so commonly found in the so-called fibrinous hydrops of the tendon-sheaths, or hygroma of the flexor tendons of the hand, always indicated a synovial tuberculosis. Another important paper on the same subject was published by Beger, who reports 4 cases that occurred in the clinic at Leipzig. The chronic tendo-vaginitis, or compound ganglia of the old authors, has been shown to be, on careful clinical observation, microscopic examination, and bacteriological research, cases of local tuberculosis. The extension of tubercular processes along tendon-sheaths from a tubercular joint after perforation of the capsule has, for a long time, been known to occur, but as a primary lesion it has only recently been added to the long list of surgical lesions of a tubercular character. As compared with other tubercular affections, primary tendon-sheath tuberculosis is quite rare, as it constitutes only 1 or 2 per cent. of the cases in the statistics of local tubercular lesions. When this affection occurs primarily and independently of tuberculosis of an adjacent bone or joint, infection with the bacillus of tuberculosis takes place by localization of floating microbes in some small vessel, and subsequently the pathological processes in the tendon-sheaths resemble those of tubercular joints. In some cases the products of the disease are massive granulations that occupy the inner surface of the tendon-sheaths; in others the granulations are less abundant, but a copious synovial exudation is thrown out; while in a third class the granulations form hard, white masses, the so-called *corpora oryzoidea*, which either remain attached to the inner surface of the sheath, or, after their separation, are found as loose bodies. In the form of tendovaginitis which corresponds with the fungous variety of tubercular synovitis, the granulations form a layer of from 1 to 4 lines in thickness upon the inner surface of the sheath. The tendon itself is covered with a somewhat thinner layer of granulation tissue, the granulations penetrating the substance of the tendon between the bundles of connective-tissue fibres, where, by absorption and pressure atrophy, they cause extensive destruction of tissue. In this manner the tendon becomes so much weakened that it ruptures on the slightest traction, or, if the disease has progressed still farther, the loss of continuity becomes complete without a trauma. The intrinsic tendency of the disease consists in progressive extension by continuity of structure along the course of the tendon primarily affected, and when this tendon is part of a compound tendon the disease gradually creeps from tendon to tendon until all the sheaths are involved. As this affection is met with most frequently in the tendon-sheaths surrounding the carpus, and as these sheaths are not infrequently in direct communication with the wrist-joint by means of small synovial sacs, it extends to the joint by continuity of surface. When no such direct connection exists between the tendon-sheath and the subjacent joint, the joint may become secondarily involved after the granulations have perforated the capsule. Next to the region of the wrist-joint the tendo Achillis, the patellar, and other tendons about the knee-joint are most frequently affected. In tuberculosis of the sheaths of the tendons of the deep flexors of the fingers the swelling is often large, extending from the lower portion of the palm of the hand underneath the annular ligament to the middle of the forearm. Underneath the annular ligament the swelling is constricted by this structure, which gives rise to considerable bulging in the palm of the hand and over the lower anterior aspect of the forearm. The fluctuating wave can be distinctly felt above and below the annular ligament, showing that the two swellings are in direct communication. The tubercular product undergoes the same pathological regressive changes as in synovial tuberculosis. If a sufficient number of tubercle bacilli is present in the granulation tissue the cells are destroyed by coagulation necrosis and caseation, the fungous masses breaking down into an amorphous, granular detritus. At this stage perforation of the tendon-sheath may take place in an outward direction, and a subcutaneous tubercular abscess develops. If such abscess open spontaneously, or is incised without regard to antiseptic precautions, infection with pus-microbes will lead to acute suppurative inflammation, which will often result disastrously from rapid extension of the phlegmonous inflammation and septic infection. The occurrence of rice-bodies in tendon-sheath and synovial tuberculosis can be traced to a specific action of the bacillus of tuberculosis on the tissues. König attributes to this bacillus properties which place it among the agents that produce fibrinous inflammation. The rice-bodies in the tendon-sheaths, the seat of a chronic inflammation, he considers as the product of a fibrinous inflammation caused by the action of the bacillus of tuberculosis. Nicaise, Poulet, and Villard examined 4 cases of hygroma containing rice-bodies, and found in all of them the bacillus of tuberculosis.

Symptoms and Diagnosis.—Tuberculosis of the tendon-sheaths is an exceedingly chronic affection. The disease is not painful, and patients often continue to follow their occupation after a number of tendons have become involved and the swelling has reached considerable dimensions. The swelling increases in length in the direction of the tendon first affected, and if the disease extend to neighboring sheaths it branches out in the direction of the tendons affected. In 9 out of 10 cases it attacks a flexor or extensor tendon in the region of the wrist-joint, and then extends upward and downward in the direction of the tendons. In tubercular hydrops of the tendon-sheaths the swelling often attains great size. In one such case I found the palm of the hand the seat of a swelling, the size of a large orange, that communicated with a smaller swelling above the annular ligament of the wrist-joint. In the fungous variety the swelling imparts to the palpating finger a semi-elastic resistance, and fluctuation is either entirely absent or not well marked. The disease often extends to the middle of the forearm, and in this locality attacks the muscular tissue in the same manner as the tendons farther below. Extension to a joint is attended by symptoms that point to synovial tuberculosis. The symptoms are so characteristic that a correct diagnosis can often be made on first sight. The only affections that must be excluded are the ordinary ganglion of tendon-sheaths and acute plastic tendo-vaginitis. A ganglion always remains as a circumscribed swelling without manifesting any tendencies to extend. The contents of a ganglion are a gelatinous mass, of the color and consistence of clarified honey. After evacuation of the sac no swelling remains, as the cyst-wall is not much thickened. A plastic tendo-vaginitis, resulting from injury or overexertion, is an acute affection not attended by much effusion or inflammatory exudation. The tendon-sheath is abnormally dry, giving rise to friction-sounds which can be plainly felt and often heard as the tendon moves within the inflamed and roughened sheath.

Prognosis.—Spontaneous cure is the exception, progressive extension the rule. The danger from regional extension arises from the tendencies of the disease to invade adjacent joints, and to extend from tendon to tendon, and finally along these to the respective muscles. There is no reason why, occasionally at least, tendon-sheath tuberculosis should not be followed by pulmonary or general tuberculosis in consequence of secondary infection.

Treatment.—The use of external applications, compression and aspiration, are of doubtful utility in the treatment of this affection. Subcutaneous evacuation, followed by iodoformization, promises more, especially in cases of tubercular hydrops with few or no rice-bodies. As the rice-bodies contain the essential cause of the disease, it will usually be found necessary to remove them in order to effect a permanent cure. Removal of these bodies, as well as extirpation of the granulation tissue, can only be accomplished by a radical operation. A radical operation has for its object the removal of all of the infected tissues, which means extirpation of the tendon-sheath and erasion of the granulations that have invaded the tendon. No operation should be undertaken unless the surgeon can count with almost positive certainty upon aseptic healing of the wound. Infection with pus-microbes under such circumstances would not only prevent a satisfactory functional result, but would place the patient's life in great peril. Fortunately, this form of surgical tuberculosis attacks localities where the surgeon has it in his power to obtain, almost with absolute certainty, an aseptic healing of the wound. Extirpation of a tubercular tendon-sheath is a tedious and difficult task. The operation must be made with the nicety of a dissection in the anatomical room. A large tenotomy knife and a small pair of curved scissors are the most useful cutting instruments in making the dissection. A number of small tenacula and toothed dissecting forceps are necessary to retract tendons and expose the parts fully to view. Esmarch's constrictor is an indispensable aid, as it renders the parts perfectly bloodless, which enables the operator to identify the parts concerned in the dissection. After the antiseptic precautions have been completed with the greatest care, the limb is rendered bloodless and the tendon-sheath is fully exposed by free external incision, which should reach on both sides a little beyond the visible limits of the disease. The tendon-sheath is now slit open, and the fluid contents are washed away by an antiseptic irrigation.

In operating upon the flexor tendons of the hand and fingers, it often becomes necessary to divide the annular ligament, which can be done without fear of impairing the functional result, as, after the operation on the tendon has been completed, its continuity can be restored by a number of separate buried sutures. The large arteries and nerves are, of course, carefully avoided. In order to remove the tendon-sheath completely, it becomes necessary to liberate the tendon and to have it drawn out of the way by an assistant. The removal of the deep portion of the sheath requires special care, as it often is in close proximity to the underlying joint, which should not be opened unless the disease has invaded the capsule deeply. The extension of the disease to the muscular tissue can be readily ascertained from the naked-eye appearances of the muscle, which, if affected, presents a grayish appearance, and is firmer than in a normal condition. If the tendon is extensively infiltrated its size is often much diminished by the removal of the infected portion, which must be done with a sharp tenotomy knife. If several tendons are affected, and access to the more remote ones is rendered impossible without division of the more superficial tendons, these can be divided and again united after the dissection has been completed. I have repeatedly spent two hours in an operation for tendon tuberculosis in the wrist-joint region, and have always felt that the time was well spent, as a hasty operation is often attended by unnecessary injury to contiguous parts, and is frequently followed by local recurrence on account of incomplete removal of the infected tissue. Should it become necessary to resect a portion of a tendon on account of extensive disease of this structure, restoration of continuity must be effected by an autoplastic operation. The tendon-end most suitable for this purpose is selected. The tendon is cut through one-half at a distance from its cut end which corresponds with the length of the defect, when it is split toward the cut end to within a few lines, and the piece is then laid over the defect and sutured at both ends. After the removal of the infected tissues the wound is irrigated once more with an antiseptic solution, dried, and iodoformized. The deep fascia is united separately with buried sutures, and the skin is coaptated accurately with interrupted stitches and the continued suture. A catgut capillary drain is inserted and a copious antiseptic dressing applied. The limb is placed upon a well-padded splint, and, if no indications for a change of dressing arise, the first dressing is allowed to remain from two to three weeks, when the wound will be found healed throughout. The functional result is almost always satisfactory if the wound heals by primary union. Massage and passive motion are instituted as soon as the wound is healed. If the operation is done early and with the necessary care, a local recurrence is not to be expected. For the purpose of illustrating the pathological conditions and the clinical tendencies of this disease, I will briefly describe one of the many cases of tendon-sheath tuberculosis that have come under my observation. This case is remarkable on account of the rapid extension of the disease. The patient was a man 60 years of age, laborer, and addicted to intemperate habits. I examined him in consultation with his family physician, about four months before the operation was performed. At that time I found an oblong swelling on the dorsum of the right hand, corresponding to the location of the extensor tendon of the index finger. The swelling was not painful, and but little tender on pressure. Fluctuation was well marked ; on deep pressure movable bodies could be distinctly felt, which were recognized as corpora oryzoidea. An operation was advised, but was declined, as the patient was still able to follow his occupation. The swelling was first noticed six weeks before the examination, but steadily increased in size. Four months later he was admitted into the Milwaukee Hospital, as the pain and the size of the swelling now disabled him from performing manual labor. At this time the dorsum of the hand corresponding to the index and middle fingers and the radial aspect of the forearm as far as the middle presented a continuous swelling, with well-marked fluctuation. The swelling had lately become painful, and was tender on pressure. Under strict antiseptic precautions the swelling was incised in its entire length, and a large quantity of synovia-like fluid and softened rice-bodies escaped. The sheaths of the extensor communis digitorum and extensors of the wrist were found lined with a thick layer of fungous granulations, and near the annular ligament numerous free and attached rice-bodies were found. The tendon-sheaths were carefully dissected out, and the whole wound, after thorough disinfection, was dusted with iodoform, drained, and sutured. A copious dressing of iodoform gauze and sublimated moss was applied, and the forearm and hand fixed upon an anterior splint. Healing of the wound by primary intention. Almost complete restoration of function. No return after two years, and patient able to perform hard manual labor. Inoculations of the fluid upon potato remained sterile. Cultivation upon coagulated hydrocele-serum showed, after a few weeks, a scanty culture of the bacillus of tuberculosis. Implantation of one of the rice-bodies into the subcutaneous connective tissue of a guinea-pig resulted in a typical tuberculosis, starting from the point of inoculation, spreading to adjacent lymphatic glands, and finally resulting, in six weeks, in death from diffuse miliary tuberculosis.

FASCIA TUBERCULOSIS.

The bacillus of tuberculosis has a special predilection for fascia, and primary localization in this tissue is a frequent occurrence. It is a well-known clinical fact that, as soon as a deep tubercular focus in a lymphatic gland, bones, or joints has reached the connective tissue outside of the organ primarily affected, the infection travels along the connective tissue, often resulting in extensive destruction of this tissue before the process reaches the surface. The extension of tubercular abscesses along preformed connective-tissue spaces has been previously described. If the tubercular product, when it reaches the loose connective tissue, is composed of living embryonal tissue, the pathological lesions which are later produced in the connective tissue correspond with those of the primary lesion. The connective tissue is transformed into masses of granulation tissue, which remains in this state for a long time before it is destroyed by coagulation necrosis, with subsequent cell disintegration. In primary tuberculosis of the fascia the disease often spreads with great rapidity, dipping down between the muscles along the intermuscular septa, and invading from here the muscles themselves. I have seen a number of cases during the last few years where the disease originated primarily in the deep fascia of the thigh, resulting in the most extensive regional dissemination in the course of two or three years. In one case, a veteran of the late war, 55 years of age, the disease commenced at a point between the greater trochanter and the crest of the ileum several years before he came under my observation. I found the thigh moderately swollen with several prominences from the crest of the ileum to the knee-joint, where fluctuation was quite distinct. I mistrusted a primary osteo-tuberculosis, but, on making free incisions at different points, I found no evidences of primary tuberculosis of any other tissue or organ. The deep fascia and intermuscular septa were found destroyed, and in their place masses of granulation tissue presenting foci of coagulation necrosis and caseation invading extensively the muscular tissue. Volkmann's spoon was freely used, but I soon found that this treatment was utterly inadequate to remove all of the infected tissue, as the deep muscles throughout were extensively infiltrated. Amputation was out of the question, as the gluteal region as far as the crest of the ileum was so extensively affected that it would have been impossible to obtain a covering for a hip-joint amputation. Iodoformization of the enormous spaces made by scraping out the fungous granulations had no effect in arresting further extension of the disease. The patient died, three months later, of general miliary tuberculosis.

In a second somewhat parallel case the disease extended from near the knee-joint as far as the trochanter minor. This patient was only 25 years of age, and the disease had existed a year and a half. Several incisions had been made, and a number of fistulous openings were found in communication with large cavities between the deep muscles of the thigh. The sinuses were laid open and scraped, and the most careful examination failed in disclosing a primary osteal or tendon-sheath tuberculosis. The muscles were again found extensively infiltrated and of a grayish-white color, and almost of gristly hardness on being incised. The operation rather hastened than retarded the progress o and I was forced, a few weeks later, to amputate the thigh just below the trochanters. The patient made a slow recovery, but at the present time, two years after the operation, he is in fair health, and there is nothing to point to a local recurrence. I have learned to regard fascia tuberculosis affecting the intermuscular septa of the thigh as an exceedingly grave form of local tuberculosis, and, if at all extensive, only amenable to successful treatment by amputation.

TUBERCULOSIS OF MOUTH AND TONGUE.

We have now every reason to believe that many cases of ulceration of the tongue, pharynx, and cavity of the mouth, which have been heretofore diagnosticated and treated as carcinoma, were not carcinoma, but syphilis or tuberculosis. Professor von Esmarch, in a very able paper, has recently again called attention to the difficulties in the way in differentiating between these affections.

Pathology.—There is no doubt that many reported cases of permanent recovery, after removal by operation of ulcerating swellings of the tongue, were not cases of carcinoma, but tuberculosis. Lupus of the pharynx and tongue are cases of local tuberculosis. Only a few weeks ago I had an opportunity to examine a case of primary tuberculosis of the pharynx occurring in a man 30 years of age. The disease had existed for four months, and involved the posterior wall of the pharynx, and had extended to the left tonsil. Ragged, deep ulcers had formed, which were covered with flabby, yellowish-gray granulations. Numerous minute miliary nodules could be seen in the mucous membrane around the ulcers, and on scraping away the granulations they were also found present in the softened, inflamed tissues underneath the floor of the ulcers. A beginning hoarseness indicated that the disease was extending by continuity of tissue to the larynx. Laryngoscopic examination revealed numerous minute nodules, which studded the mucous membrane of the posterior surface of the epiglottis. The recent advances made in the microscopical, bacteriological, and experimental methods of examination have succeeded in separating from syphilitic affections and malignant disease of the mouth and tongue many cases that belong to the long list of affections now classified under the head of surgical tuberculosis. The cavity of the mouth is often the seat of slight abrasions and pathological conditions, which may become an infection-atrium for the entrance of micro-organisms that might be contained in the air we breathe, the food we eat, and the water we drink. Remembering the frequency with which superficial abrasions and ulcerations occur in this locality, it is not strange that primary tuberculosis should occasionally develop here. The tubercle bacillus produces the same tissue changes here as on the surface of the skin, the primary pathological product consisting of granulation tissue undergoing molecular retrograde tissue metamorphosis, followed by ulceration. Ulceration is an earlier occurrence, and a more conspicuous clinical feature in tuberculosis of the mouth than in some other localities, as the new tissue is constantly macerated by the fluids with which it is moistened at all times. The tubercular ulcer is generally covered by the products of interstitial necrobiosis and superficial coagulation necrosis, which result in the formation of what appears as a false membrane. If this membrane, when present, is removed, the characteristic granulation surface is exposed. The ulcer is surrounded by a zone of inflammatory infiltration, which, however, does not present the same feeling of hardness as carcinoma. The most characteristic feature of a tubercular ulcer of the mouth or tongue consists in the presence of minute tubercle-nodules in the margins and underneath the layer of granulations, and, if the infection has extended to some distance, in the surrounding mucous membrane. Schliferowitsch has published an exhaustive *résumé* of the literature on this subject to date, and has collected all the recorded cases in which the diagnosis of tubercular disease of the cavity of the mouth could be made with some degree of certainty. The cases number 88, and included those of primary and secondary tuberculosis. From a careful study of this affection he has come to the conclusion that it occurs seldom in the very young, and that it attacks most frequently persons between 40 and 50 years of age.

Symptoms and Diagnosis.—Tuberculosis of the mucous membrane of the cavity of the mouth appears as a flattened, submucous infiltration composed of granulation tissue, which, at an early date, becomes the seat of a superficial ulceration in the centre that rapidly extends toward the margins of the swelling. Caseation is seldom observed. The cells are destroyed by coagulation necrosis, and as they become detached the defect increases in size. The appearance of the ulcer in this locality is characteristic. If on the tongue, it is found on the borders near the tip of the organ. It appears as an oblong ulcer, with raised, ragged borders of firmer consistence, showing the color of fresh granulations. The ulcer often appears as if covered by a pseudo-membrane; if this covering is removed, the surface left easily bleeds. The surface of the ulcer is uneven, as if covered with hypertrophic papillæ. The discharge of pus is slight, and, in many cases, miliary nodules may be found around the ulcer. Pain is not as severe as in carcinoma. Lymphatic glands may become secondarily infected, but this is not often the case. In the primary form of the disease. when a positive diagnosis is most difficult, the presence of tubercle ba li [illegible] f the ulcer.

A gumma of the tongue, as a rule, develops into a larger swelling than a tubercular affection before ulceration takes place, and the resulting ulcer is more deeply excavated; at the same time, other evidences of syphilis can usually be detected. Miliary nodules in the immediate vicinity of the ulcer are absent in a syphilitic ulcer, and frequently present in tuberculosis. If any doubt remain as to the differential diagnosis between these two affections, this should be set aside by a course of antisyphilitic treatment before resorting to any serious operation. If the ulcer is syphilitic it will heal kindly under such treatment, while no improvement will be noticeable if it is tubercular. Epithelioma commences as a superficial infiltration and penetrates the tissues from without inward. Induration around and underneath the ulcer is more marked in an ulcerating epithelioma than in a tubercular ulcer. Glandular infection takes place early, and is almost a constant occurrence in epithelioma, but is seldom observed in the course of a tubercular ulcer. A simple ulcer of the tongue caused by the mechanical irritation from a sharp projection of a carious or displaced tooth can be readily recognized by the location and character of the ulcer. Such an ulcer may become the seat of a tubercular ulcer or the starting-point of an epithelioma.

Treatment.—The local treatment of a tubercular ulcer of the mouth or tongue is the same as when a similar ulcer is located upon the surface of the body. If the lesion is circumscribed sufficiently that the wound, after complete excision, can be closed by suturing, this method of treatment should be adopted, as it is certainly the most radical, and results most speedily in complete recovery. If the extent of the disease render this treatment inapplicable, the diseased tissues should be removed as thoroughly as possible by a vigorous use of the sharp spoon, or by destroying it with the actual cautery, or both of these measures may be combined. The use of superficial caustics has a tendency rather to aggravate the disease than to cure it. With a sharp spoon all of the soft tissues are scraped away, the healthy tissue being recognized by its greater firmness and resistance to the spoon. After bleeding has ceased, the surface is cauterized with the flat point of a Paquelin cautery, and, if the disease has dipped in farther at certain points, these are attacked by making ignipuncture with the needle-point. The cavity of the mouth, during the after-treatment, must be kept as nearly as possible in an aseptic condition by dusting the surface daily with iodoform, and by the frequent use of a mild, antiseptic mouth-wash, such as a saturated solution of acetate of aluminum or boric acid. If all the infected tissues have been destroyed, healing takes place rapidly by granulation, cicatrization, and epidermization after separation of the eschar. If any of the infected tissues have remained, the process of healing is retarded or completely arrested; in the latter event, a repetition of the same local treatment will become necessary.

TUBERCULOSIS OF THE MUCOUS MEMBRANE OF THE INTESTINES.

Primary tuberculosis of the intestinal mucous membrane is a comparatively frequent affection, but becomes a surgical lesion only in case it leads to intestinal obstruction or perforation. If, as is sometimes the case, the infection is limited to a single focus, a timely operation not only relieves the symptoms which made surgical treatment a necessity, but it may result in a permanent cure. The tubercular lesions of the intestinal mucous membrane that occasionally indicate treatment by laparotomy are usually found in the lower portion of the ileum, the ileo-cæcal region, cæcum, or ascending colon. Tubercular inflammation of the large intestine may cause so much swelling as to give rise to intestinal obstruction. When the inflammatory process is limited to a small portion of the bowel, operative removal of the affected segment is justifiable, and holds out a fair prospect of permanent relief. Schier reports a successful case of this kind. At the close of October, 1887, he was consulted by a man who had a painful swelling in the right hypochondrium; the swelling was as large as a man's fist, with a nodular surface. Considerable pain, tenderness, emaciation, and evidences of intestinal obstruction, which were gradually increasing in integrity. A tumor of the cæcum was diagnosticated, and laparotomy was performed November 1st of the same year. The abdomen was opened by a lateral incision. The omentum near the swelling was much inflamed and covered with whitish-yellow nodules, from the size of a pin to that of a pea. Twelve to sixteen enlarged glands, some as large as a walnut, situated along the vertebral column, were enucleated or removed with a sharp spoon. The cæcum was so fragile that it ruptured during the manipulations and some fæces escaped. The bowel above and below the swelling, which involved the cæcum, was emptied by expression, tied with rubber bands, and the affected portion excised. The part of the cæcum containing the valve and the vermiform appendix was left. Circular suturing by a double row of sutures. The subsequent history of the case was favorable in every respect. Pain was severe for two days, and yielded to large doses of opium. Eighteen months after the operation the patient remained in good health. Examination of the part removed showed that the swelling was of a tubercular nature, the submucosa and external layers of the bowel being mainly involved.

Durante [illegible] ewhat similar case. The patient was a woman. [illegible] lve years, had suffered from obscure pain in the right iliac fossa when at stool. The pain increased in intensity and became paroxysmal, and the patient almost starved herself with the object of avoiding the torture of defecation. On examination a tumor was found in the right iliac fossa, extending downward toward the upper outlet of the pelvis. Carcinoma of the cæcum or neighboring parts was suspected. The abdomen was opened. The swelling, as large as a lemon, was found adherent to the iliac fossa, the parietal peritoneum and coils of the small intestine being matted to it so firmly that the lower end of the latter, measuring 25 centimetres in length, together with the cæcum and a portion of the ascending colon, were removed with it. The two ends of the divided intestine were brought together by three rows of sutures. The abdominal wound was closed, and the patient made a rapid and permanent recovery. The swelling, which had almost completely blocked up the lumen of the intestine, was found to be of a tubercular nature. If, in cases of intestinal tuberculosis indicating laparotomy, it should be found, after opening the abdomen, that the foci in the ileo-cæcal region are too numerous to warrant a radical operation by enterectomy, the symptoms can be relieved and the inflamed parts excluded from the fæcal circulation by establishing an anastomosis between the intestine above and below the affected segment by means of decalcified, perforated bone-plates.

TUBERCULOSIS OF THE MAMMARY GLAND.

A number of well-authenticated cases of primary tuberculosis of the mammary gland have recently been reported. So far as the infection is concerned, the breast must be considered as an appendage of the skin. The bacillus from without may effect entrance into the gland through the milk-ducts, in which case the inflammatory process commences in the parenchyma of the gland; or it may enter through a fissure of the nipple, in which case the process is primarily interstitial. When direct infection from without can be excluded, the disease is the result of auto-infection, and on this account the prognosis is always more unfavorable. Regional dissemination takes place along the chain of axillary lymphatic glands. Orthmann examined the enlarged lymphatic glands in a case of primary tuberculosis of the mamma, and found numerous tubercle bacilli. The disease is differentiated from carcinoma by the absence of pain and hardness in the swelling, and from an ordinary suppurative mastitis by the absence of the prominent symptoms of acute inflammation. It might be mistaken for a lacteal cyst or an echinococcus-cyst, but all doubt as to the nature of the swelling can be set aside by an exploratory puncture.

Treatment.—The more expectant plans of treatment recommended in the management of tubercular abscesses communicating with the primary foci in tissues and organs deeply situated should not be followed in the treatment of tubercular affections of the breast, as in these cases a radical operation is not attended by any danger to life, and usually results in a permanent cure. The plan to be pursued depends on the extent and location of the disease. A superficial limited tubercular focus of the mamma can be successfully treated by excising the infected tissues. If the process is more deeply located, it may become necessary to remove a portion of the mammary gland with it. Partial excision of the gland should be done in such a manner as to include the tubercular focus in a wedge-shaped section of the gland, the base of the wedge being directed toward the periphery of the gland. After excision the cut surfaces of the gland are united with buried catgut sutures. If the disease has infiltrated the gland extensively, or if a number of sinuses have formed, it becomes necessary to extirpate the entire gland. Enlarged glands are removed in the same thorough manner as in operating for carcinoma of the breast.

TUBERCULOSIS OF THE GENITO-URINARY ORGANS.

It is only within the last few years that a number of chronic inflammatory processes of the genito-urinary organs in both sexes have been shown to be tubercular in their origin, clinical tendencies, and final termination. The susceptibility of the mucous membrane of the genito-urinary tract to tubercular infection has been demonstrated experimentally by Cornet. In rubbing a pure culture of tubercle bacilli in superficial abrasions of the penis in dogs, he produced a tubercular lesion of that organ. In bitches, tuberculosis of the vagina and uterus could be produced by injection of a pure culture into the vagina. The local lesions were followed by general tuberculosis.

(a) Tuberculosis of Vulva, Vagina, and Uterus.—Direct tubercular infection of the genital tract in women has been observed, but the cases so far reported are few. Barbier believes that a woman can be infected by a tuberculous man during coitus, as bacilli have been demonstrated in the semen of tuberculous patients, as well as in the discharge attending tubercular epididymitis. The uterus may be infected by extension from a tubercular lesion of the vulva without any intermediate trace of infection in the vagina. The author even admits the possibility that tubercular infection may be transmitted by the finger of the attendant, by infected instruments, or even through the medium of the air. Zweigbaum reports a case of primary tuberculosis of the portio vaginalis uteri, which, at the time of examination, appeared in the shape of an ulcer the size of a walnut, with thick, indurated margins and cheesy floor.

Numerous tubercle bacilli were found in the secretion taken from the surface of the ulcer. Evidences of tuberculosis were apparent at this time. After a few weeks the ulcer extended toward the left vaginal wall and left labia majora. A section of a fragment of tissue removed from these parts, on staining, showed numerous bacilli. This form of tuberculosis is not frequent, as the author could find only 2 cases of vulvo-tuberculosis in literature, although genital tuberculosis is quite a frequent affection. Jonin believes that tubercular endometritis from local infection is quite a common affection. Of 9 cases which were observed by him it was due to sexual contact with men suffering from genital tuberculosis. In 2 others the husbands were tuberculous, but had no genital tuberculosis. He calls attention to the fact that Cornil and Chantemesse have produced this disease artificially in rabbits by injecting bacilli into the vagina. The cases of primary tuberculosis of the vulva, vagina, and uterus will undoubtedly become more numerous in the literature of the near future, when improved methods of examination will enable the surgeon to make a positive diagnosis between these affections and carcinoma and syphilitic lesions. The same points in differential diagnosis are to be remembered in this connection as have been enumerated in the consideration of tubercular affections of the mouth.

Treatment.—Primary tuberculosis of the utero-vaginal canal and vulva should be treated by curetting, and, if the extent of the lesions make it necessary, by cauterization with the actual cautery. Before either of these procedures are put into practice, the parts must be rendered aseptic by antiseptic irrigation. Subsequent infection can be guarded against by the free use of iodoform, and tamponade of the vagina with iodoform gauze. Under ordinary circumstances, it is not necessary to remove the tampon oftener than once a week, when the surface is again freely dusted with iodoform before a new tampon is inserted.

(b) Tuberculosis of Fallopian Tubes.—In the absence of tubercular lesions of the vagina and uterus, it is doubtful if infection of the Fallopian tubes can take place by the entrance of the bacillus through the genital tract, and the relatively frequent occurrence of the disease in that part of the genital tract is only explainable by attributing it to auto-infection, in the same way as we have explained the occurrence, for instance, of primary tuberculosis of joints, bone, and peritoneum. We can safely assert that tubercular infection of the Fallopian tubes often, if not always, takes place upon the basis of pre-existing pathological conditions, taking it for granted that the healthy tubes do not present favorable conditions for the localization of the tubercle bacilli. A catarrhal condition of the mucous membrane lining the tubes, as in other organs, undoubtedly furnishes, in many instances, the *locus minoris resistentiæ* for the localization of bacilli brought to the part through the circulating blood.

An interesting case of primary tuberculosis of the Fallopian tubes has been recorded by Kotschau. The patient was 45 years old, having a good family history; has suffered for a year with pains in the abdomen, profuse metrorrhagia, and various nervous disturbances. She was treated for retroflexion, and subsequently had an attack of pelveo-peritonitis. Vaginal examination disclosed a firm, smooth, movable swelling, as large as an apple, to the right of the uterus; this was taken for a malignant ovarian growth, and laparotomy was done for its removal. On opening the abdominal cavity, a quantity of turbid, purulent fluid escaped. The swelling, of oblong shape, was found lying apparently in a bed of pus; on account of its intimate adhesions it could not be removed. The patient died from shock. The autopsy showed the uterus enlarged and retroverted. The right tube was tortuous and generally thickened. Near its distal end it was dilated into a swelling the size of a hen's egg, in the centre of which was a cavity containing cheesy material. Other smaller caseous foci were found in the tubal wall in close proximity to the large swelling. The ovary on the same side was enlarged and transformed into a caseous mass. The left tube and ovary showed similar changes, though less extensive. The microscopic examination of the pathological product confirmed the diagnosis of tuberculosis. Although the disease appears to have been primary in the tubes, the affection occurs more frequently from the direct extension of a tubercular endometritis to the tubes. Lebedeff gives a full description of a case that came under his observation. The patient was the widow of a man who had died of pulmonary tuberculosis. An examination before the operation revealed a firm, nodulated, intra-abdominal tumor in the space of Douglas. An attempt was made to remove the tumor by laparotomy, but had to be abandoned, as the disease had become too widely disseminated. Six weeks later the patient died with symptoms of general tuberculosis. At the post-mortem miliary tuberculosis was found in the peritoneum, lungs, colon, uterus, and Fallopian tubes. The most advanced stages of the disease were found in the uterus and Fallopian tubes, showing that the disease had commenced in these organs. Both of the Fallopian tubes were dilated and filled with pus, the epithelium in parts being absent. Stained sections from the uterus and tubes showed the presence of numerous bacilli.

Symptoms and Diagnosis.—Tubercular salpingitis, occurring as a secondary lesion to a primary tuberculosis in the lower portion of the genital tract, can be suspected if, in connection with a cervical or endometritic tuberculosis, examination reveal a swelling in the region of one or both Fallopian tubes. Primary tubercular disease of the Fallopian tubes gives rise to local conditions and symptoms that it would be impossible to differentiate from an ordinary pyosalpinx. The existence of a dilated, inflamed Fallopian tube can generally be made out with some degree of certainty by making the examination while the patient is under the influence of an anæsthetic. Werth has described an acute and chronic form of tubercular salpingitis. In the acute variety both the muscular and serous coats undergo caseous degeneration, numerous bacilli being found in the interior of the tube; while in the chronic form the wall of the tube undergoes thickening and infiltration with new cells, and its contents contain only a few bacilli. The increase in size of the tube is due to the collection of pus in its interior as well as to the thickening of the wall. When suppuration takes place in the interior of the tube the tubercular product has become the seat of a secondary infection with pus-microbes; hence, indications for operative treatment have become more urgent. If the tubercular inflammation extend from the abdominal extremity of the Fallopian tube to the peritoneum, symptoms of tubercular salpingitis are obscured later on by those of tubercular peritonitis.

Treatment.—As a tubercular salpingitis calls for the same treatment as a pyosalpinx, it is, for all practical purposes, only necessary to narrow the diagnosis down to either one of those two affections before resorting to treatment by laparotomy. A median incision is preferable to a lateral, as frequently both tubes are affected simultaneously. Salpingectomy should be combined with oöphorectomy, as the ovaries are frequently implicated in the tubercular process, and these organs would be of no further use after extirpation of the tubes. As tubercular tubes are usually found firmly adherent to the surrounding tissues, their removal is often attended with the greatest difficulties, and may become an impossible task. If the disease is limited to the tube-structures, and has not involved surrounding important organs, it would appear rational, under such circumstances, to lay the tube open, remove its contents, scrape out the infected tissues as far as possible, arrest bleeding by applying the actual cautery, and, after thorough iodoformization, pack with iodoform gauze. This treatment would certainly appear more rational than to be content with an exploratory incision, and allow the patient to remain a sufferer until relieved by death from tuberculosis. In one case that came under my treatment, where both tubes were imbedded in a mass of granulation tissue, I was unable to remove the entire mass, was compelled to pursue this course, and the patient recovered quickly and permanently, in spite of a fæcal fistula that formed a few days after the operation.

TUBERCULOSIS OF GLANS PENIS AND URETHRA.

Kraske has observed a case of tubercular ulceration of the urethra, extending from the membranous portion to the neck of the bladder, in a patient, 33 years of age, who was treated for chancre. The autopsy revealed advanced tuberculosis of the genito-urinary tract and pulmonary tuberculosis. In another case, a man 49 years old, a tubercular ulceration existed on the dorsum of the glans the size of a cent piece. This sore was also mistaken for a primary lesion of syphilis. There were no signs of pulmonary tuberculosis. The glans was amputated, when it was observed that the tubercular infiltration extended deeply into the cavernous structure. The lesion could not be traced to genital contact, and under the microscope showed the typical structure of tubercular tissue. In the examination of doubtful lesions of the glans penis, it is well to remember the possibility of tubercular infection in this locality, and, in case the tubercular nature of a lesion can be established on sufficient grounds, to resort to cauterization with the actual cautery, excision, or amputation, according to the location and extent of the disease.

TUBERCULOSIS OF EPIDIDYMIS AND TESTICLE.

In the male genital apparatus tuberculosis attacks most frequently the epididymis, for the reason that the vessels in this structure are more tortuous and smaller than in the remaining portion of the testicle or the vas deferens, both of which are important elements in determining localization in that part from floating bacilli that reach it through the circulating blood. Saltzmann states that these anatomical conditions are important factors in the arrest and localization of floating bacilli. That in cases of tuberculosis of the testicle we are only dealing with an external manifestation of an antecedent infection becomes apparent by the clinical observation that not infrequently both testicles are infected, either simultaneously or some time apart, showing that the infection came from the same source. Tuberculosis of the genital organs in the male furnishes one of the best examples of the typical clinical course of local tuberculosis. The disease extends by continuity of structure often to a great distance from its starting-point. Nothing is more familiar than the clinical course of a case of tuberculosis of the testicle. A small, hard nodule is first detected in the epididymis, and from this point the whole structure of the epididymis is infected, when the infection slowly, but surely, extends to the testicle; then along the vas deferens to the vesiculæ seminalis, the prostate gland, and bladder, and from this viscus along the ureters to the pelvis of the kidney. As a rule, the disease remains limited to the genito-urinary organs, but in some instances metastatic infection takes place, either from the genito-urinary organs or from the primary source of infection. A gentleman was recently under my care whose case illustrates a number of interesting points descriptive of the clinical behavior of genital tuberculosis. He was 35 years of age; married for ten years; the marriage had been childless. He claimed that he never had syphilis or gonorrhœa. Tuberculosis is hereditary in the family. Nine years ago he noticed a small, hard swelling in the epididymis of both testicles. Two years ago symptoms of cystitis appeared, which were not much improved by internal medication and antiseptic irrigation of the bladder. Six months ago his left knee became swollen and painful. Four months later he commenced to suffer severe pain in the region of the left kidney. Temperature varied from 100° to 103° F. A swelling soon formed in the left lumbar region, and four weeks later I evacuated a large quantity of pus through a lumbar incision. Through the incision the kidney could be seen and felt, and, by passing the index finger around it, it appeared to be extensively separated from the contiguous structures. The left knee presented all the appearances of advanced synovial tuberculosis. No evidences of pulmonary tuberculosis. The disease in both testicles had made no progress for years, and the infiltration appears to be limited to the epididymis. The epididymis on both sides is moderately swollen and indurated. The vas deferens on each side is somewhat larger and firmer than normal. The disease had extended from the epididymis to the pelvis of the kidney on both sides, all of the intervening organs being involved in the tubercular process. The only apparent manifestation of general tuberculosis was presented by the left knee. An interesting feature in this case was the formation of a paranephritic abscess around a pyelo-nephritic kidney, which must be regarded as the result of a secondary infection with pus-microbes.

Symptoms and Diagnosis.—Tubercular epididymitis always appears as a chronic affection, in this respect differing from gonorrhœal epididymitis and the ordinary form of acute parenchymatous and suppurative orchitis. Pain and tenderness are either entirely absent or, at least, slight when present. Circumscribed hydrocele may develop as soon as the disease extends to the tunica vaginalis. The tubercular inflammation is characterized by the same pathological conditions as in other organs, new nodules appearing in the neighborhood of the first one, which, by confluence, form masses of considerable size. Caseation is an early and almost constant condition. In many cases the process extends in the direction of the skin; a tubercular abscess forms in the tunics of the scrotum; the skin presents a bluish-red color, and spontaneous perforation gives rise to evacuation of the abscess. Frequently multiple abscesses form in this manner, and the fistulous openings lead down to caseous masses. In some cases, as the one reported, the disease in the epididymis becomes latent, but the infection extends at an early date along the vas deferens, which becomes swollen and indurated, and from which, if a cross-section is made, the characteristic cheesy material can be squeezed. From the vas deferens the disease extends to the vesiculæ seminalis, prostate gland, bladder, and finally creeps along the ureters to the pelvis of the kidney, usually simultaneously on both sides. The only disease with which tubercular epididymitis might be confounded is tertiary syphilis, affecting the same part of the testicle. In cases of doubt the patient should be placed on antisyphilitic treatment for a few weeks, which, if the affection is tubercular, will produce no impression on the swelling; on the other hand, if it is syphilitic, it will rapidly diminish in size.

Treatment.—The only radical treatment in tuberculosis of the epididymis and testicle is castration. This operation is indicated if the disease is limited to one testicle, and no evidences of tuberculosis can be found in any other organ beyond the reach of surgical treatment. I have removed both testicles in two cases, but in both patients tubercular cystitis developed one and two years, respectively, after the operation, and in one of them the immediate cause of death was pulmonary tuberculosis. My own cases and the experience of other surgeons would tend to dictate a conservative course of treatment if both testicles are affected. After the disease has extended to the organs at the base of the bladder or the bladder itself, castration is, of course, positively contraindicated. The co-existence of pulmonary tuberculosis, or tuberculosis of any of the larger joints, would furnish a sufficient ground against the propriety of castration. Castration is a legitimate operation, and yields fair results if the patient is otherwise in good health and the disease is limited to one side, and has not extended along the cord beyond a point where all of the infected tissues can be removed. The tunica vaginalis should always be removed with the testicle, and, if the scrotum is adherent at any point, the adherent portions of the skin must be excised at the same time. In removing the testicle for tuberculosis, it is always necessary to carry the incision as far as the internal ring, in order to remove as much as possible of the cord. The vessels of the cord should be tied separately, as tying the cord *en masse* gives rise to unnecessary pain, and the ligature is liable to slip,—an occurrence that might be followed by troublesome hæmorrhage.

TUBERCULOSIS OF THE VESICULÆ SEMINALIS.

In 1829 Dahmar described a chronic inflammation of the seminal vesicles, the description of which corresponds closely to that of tuberculosis. Since then this affection has been described by Albers, Jaye, Naumann, Humphrey, and Kocher, and lately it has been studied by Rayer, Cruveilhier, and Reclus as secondary to pulmonary tuberculosis. As a secondary affection this ailment is not only seen in connection with tuberculosis of the lungs, but is more common after primary tuberculosis of the epididymis, either as a continuation of the cheesy degeneration in the vas deferens or spreading by contiguity of tissue from the sides of the prostate. Primary tuberculosis of these organs is extremely rare, and still less often diagnosed, and up to quite recently no surgical interference has been attempted. Ullmann now reports a case of primary tuberculosis of the right testicle, with secondary affection of the seminal vesicles on both sides, in a lad 17 years of age, where, after removal of the right testicle, he extirpated these organs through a semi-lunar incision in the perineum. The general health of the patient improved after the operation, but a small urinary fistula remained, which formed in consequence of injury to the base of the bladder during the operation. He is of the opinion that the seminal vesicles should be removed in primary tuberculosis of the testicle or epididymis, when no suspicious symptoms have appeared on the sound side, and when on the affected side the vesiculæ seminalis are already attacked; also in cases of primary tuberculosis of the seminal vesicles. The impotence following the operation should be no contra-indication, for in all reported cases of tuberculosis of the seminal vesicles impotence always occurs in a short time; in fact, it is regarded as a cardinal symptom of the disease.

TUBERCULOSIS OF THE BLADDER.

Tuberculosis occurs either as a primary or secondary affection. Several cases of well-marked primary tuberculosis of the bladder in the female have come under my observation, where the disease evidently commenced at the neck of the bladder, and, after spreading over the whole internal surface of the viscus, extended along the ureters to the pelves of the kidneys, and, finally, in the course of a few years, proved fatal from tubercular pyelo-nephritis. Primary tubercular cystitis appears to be more frequent in females than in males, undoubtedly because, on account of shortness of the urethra, direct infection is more liable to occur.

Strümpell, after a careful study of 4 cases of primary tuberculosis of the bladder in men, came to the conclusion that infection takes place through the urethra. The tubercle bacilli, finding no favorable place for localization and growth in the urethra and bladder, finally reach the prostate gland or the epididymis, the whole process resembling what occurs in inhalation tuberculosis, in which the disease manifests itself not in the mucous membrane of the bronchial tubes, but in the parenchyma of the apices of the lungs.

Symptoms and Diagnosis.—Tuberculosis of the bladder is clinically characterized by symptoms of cystitis, the intensity of the symptoms varying according to the part of the bladder affected, the extent of the disease, and the presence or absence of complications. If the disease primarily involve the neck of the bladder, tenesmus and frequent desire to urinate are the most distressing symptoms. As long as no ulceration of the vesical mucous membrane has taken place, the urine may present a perfectly normal appearance, and, on examination, is found normal in other respects. Very frequently the symptoms become very much aggravated shortly after an examination of the bladder, made upon the supposition that the patient is suffering from stone in the bladder, as the introduction of a sound without the necessary antiseptic precautions is often followed by a secondary infection with pus-microbes, which gives rise to an acute suppurative cystitis. The general health of the patient now becomes rapidly undermined, and the extension of the local disease in the direction of the kidneys is hastened. The urine contains large quantities of pus and mucus, and becomes ammoniacal from the presence and action of putrefactive bacteria. The walls of the bladder become greatly thickened from inflammatory exudation and tubercular infiltration; the organ is unable to empty itself completely, and the decomposed residual urine becomes an additional source of irritation and progressive infection. Incontinence of urine is a frequent symptom in advanced vesical tuberculosis, and is usually an indication that the organ is extensively diseased. In secondary tuberculosis of the bladder it is usually not difficult to locate the primary disease, and thus establish a positive diagnosis. The presence of tubercle bacilli in the urine in cases of primary tuberculosis of the organ furnishes a positive diagnostic criterion between ordinary cystitis and vesical tuberculosis. In the absence of ordinary causes of cystitis, such as gonorrhœa, stricture of the urethra, enlarged prostate, calculus, and tumors of the bladder, symptoms of cystitis point strongly toward a tubercular origin of the inflammation, and should induce the surgeon to make a most careful examination in reference to the etiology and nature of the cystitis. It is only by excluding the presence of the different lesions of the bladder by a careful and thorough examination of that viscus and its neighboring organs, as well as a chemical, microscopical, and bacteriological examination of the urine, that a positive diagnosis of vesical tuberculosis can be made during the early stages of the disease. Tuberculous urine injected into the peritoneal cavity of a guinea-pig will produce tuberculosis in this animal, and in doubtful cases this diagnostic measure may prove of great value.

Prognosis and Treatment.—In secondary tuberculosis of the bladder the regional infection has extended so far that even the most heroic surgical measures will necessarily fail in eliminating the disease, and death from extension of the disease to the kidneys, or from secondary pulmonary or general tuberculosis, will follow as an inevitable result. In primary vesical tuberculosis, the disease, at the time a positive diagnosis can be made, has usually invaded so much of the walls of the bladder that a radical operation would necessitate an extensive resection of its walls, after which it would be found impossible to utilize the remaining portion of the organ as a reservoir for the urine. Resection of the wall of the bladder has been done in several instances in the treatment of malignant tumors at its base, but have usually terminated in the formation of a permanent urinary fistula.

Dr. R. Harvey Reed, of Mansfield, Ohio, has recently made an interesting series of experiments on dogs, with a view to dispense with the bladder altogether in cases of extensive disease of this organ, necessitating partial or complete excision. He has shown that the ureters can be successfully implanted into the rectum, thus excluding permanently the urinary tract below this point from the urinary passages, and utilizing the rectum as a reservoir for the urine. If the operation of implantation of the ureters into the rectum can be perfected to such an extent as to become a feasible and practical procedure in surgery, it may be possible, in the future, that vesical tuberculosis can be successfully dealt with by complete excision of the affected organ.

The conservative treatment of vesical tuberculosis by injection of solutions of boric acid, benzoate of soda, the ordinary antiseptic solutions, and iodoform has little or no effect, either in affording palliation or in retarding the regional extension of the disease. Internal medicines, such as boric acid, benzoate of soda, uva ursi, buchu, and triticum repens, are of utility in relieving vesical tenesmus, before secondary infection with pus-microbes and putrefactive bacteria has occurred, by rendering the urine alkaline and more copious; but during the later stages of the disease they are useless even as palliatives. If the tubercular process is limited to the urinary passages below the ureters, incision and drainage of the bladder secure rest to this organ and open up a direct route for the more effectual treatment of the tubercular lesions, and thus not only constitute the most efficient palliative measure, but also the most effective procedure in retarding the local extension of the disease by direct vigorous antitubercular treatment. I had an opportunity to observe the palliative effect of an opening in the bladder, in a case of primary vesical tuberculosis in a female aged 35 years, where the tubercular ulceration resulted in the formation of a vesico-vaginal fistula. The tenesmus was promptly relieved, as soon as the bladder was placed in a condition of rest, by the escape of urine through the fistulous opening.

In the female the most direct route into the bladder, and affording the most efficient drainage and furnishing the most advantageous conditions for the local treatment of the tubercular lesions, is a vaginal cystotomy made near the neck of the bladder. The opening should be at least 1½ inches in length, extending from near the neck of the bladder in an upward direction. Tubular drainage should be dispensed with, as all foreign substances in the bladder not only act as irritants, but interfere with complete drainage. As the opening is made in the most dependent portion of the bladder, free drainage can be secured most efficiently by means which prevent contraction or closure of the vesico-vaginal opening. This can be done by suturing the mucous membrane of the bladder to the vaginal mucous membrane, thus establishing a permanent bimucous fistula between the bladder and the vagina. Through this opening accessible tubercular lesions can be treated by the use of the sharp spoon and the direct application of iodoform. The parts below this opening should be protected against the irritating effect of urine by applications of vaselin or lanolin containing one of the milder antiseptic remedies. After the fistulous opening has been established the bladder can be irrigated with antiseptic solutions, or a mixture containing iodoform, through the urethra.

In the male the same objects are attained most efficiently by making a suprapubic cystotomy, as through a perineal incision the direct treatment of tubercular lesions is impossible. The fistulous communication should be made complete by suturing the margins of the visceral wound to skin-flaps taken from each side of the external incision,—a method first suggested by Morris, of New York. By lining the margins of the incision with mucous membrane and skin, the loose connective tissue in the pre-vesical space is protected against infection, and the fistulous opening is rendered permanently patent. At the time of operation visible tubercular ulcers are curetted and iodoformized. The bladder can be irrigated subsequently through the urethra or through the fistulous opening.

In a case of advanced primary tuberculosis of the bladder where I pursued this method of treatment the operation afforded marked relief, but appeared to have no influence in retarding a fatal termination, as the disease had already extended to the kidneys. The patient lived for nearly two months in comparative comfort, the principal complaint made being the moisture caused by the constant escape of urine through the artificial urethra.

A case is described by Battle in which recovery followed curetting through a suprapubic incision, after the failure of less formidable means. The patient was a girl aged 20 years. The opera rmed

July 29, 1889. The patient was discharged September 20th, and April 8, 1890, was in good health and working at her trade.

In cases where the disease in the bladder is circumscribed, and the organ is opened early, the treatment might, occasionally at least, result in a permanent cure, if the infected tissues can be completely removed by curetting or destroyed by the actual cautery through the incision at the time of operation. In such favorable cases the opening should not be allowed to close until the surgeon can satisfy himself that the ulcers have completely healed, and that no new centres of infection are present.

CHAPTER XXII.

ACTINOMYCOSIS HOMINIS.

ACTINOMYCOSIS is a form of chronic inflammation caused by the presence of actinomyces or ray-fungus. Until quite recently this disease was included among the malignant tumors, and we have reason to believe that, in many of the reported cases after operations for sarcoma, the disease for which the operations were done was not sarcoma, but actinomycosis. Before degeneration of the inflammatory product has taken place actinomycosis resembles a tumor more closely than any other inflammatory swelling. The swelling is composed largely of granulation tissue, which, on examination under the microscope, presents a histological structure that, in the absence of other evidences, it would be difficult or impossible to differentiate from a round-celled sarcoma. The presence of the specific fungus in the granulation tissue settles the diagnosis.

HISTORY OF THE DISEASE.

The disease, as occurring in cattle, was first described by Böllinger, in 1877, as a condition in which sarcoma-like tumors were met with, associated with a peculiar growth which, from its structure, was named "*Strahlen pilz*" (ray-fungus), or actinomyces. James Israel was the first to recognize the disease in man, but it was not generally understood until the appearance of the classical work of Ponfick ("Die Aktinomykose des Menschen," Berlin) in 1882. Numerous articles on this subject have since appeared in the current medical literature, so that Partsch, in 1888, mentioned in his monograph seventy-five references, with a supplemental list of thirty-three names furnished by Schuchardt. Since the publication of Israel's case numerous cases have been reported by different observers, representing Germany, England, Belgium, Switzerland, Russia, Austria, France, and America; so that Partsch in his paper estimates the whole number up to that time at not less than one hundred. While most of the articles in medical journals contain only a description of isolated cases, it appears to have been the good fortune of some of the writers on this subject to meet with a number of cases in a comparatively short time. Thus, Hochenegg reports 7 cases that came under his observation, and Moosbrügger has increased the list of published cases by 10 well-authenticated and carefully recorded cases.

Rotter observed 13 cases in two years. Albert has seen not less than 38 cases of actinomycosis in man within the past few years; of these 8 have come under his observation during the last two years. These cases have come mostly from Vienna and its vicinity.

DESCRIPTION OF FUNGUS.

The ray-fungus, or actinomyces, is not, strictly speaking, a microbe, as it is large enough to be seen with the naked eye; but its identity can only be ascertained from its characteristic structure, which requires the use of the microscope. Böllinger described as peculiar to this disease certain yellow bodies, visible to the naked eye, always found in the pus of actinomycotic abscesses and in the granulation tissue before suppuration had occurred. Microscopically, they were found to consist of threads similar to the ordinary mycelium, which terminated in bulbous ends.

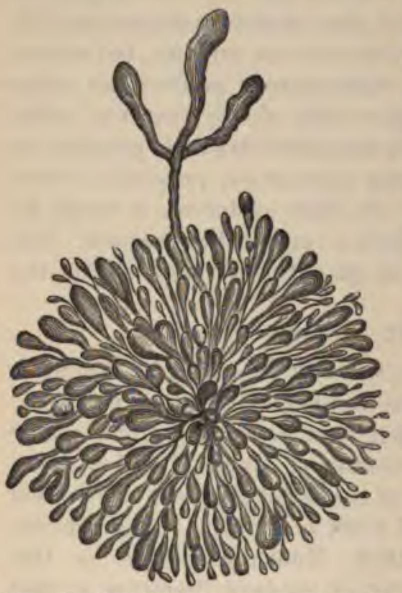

FIG. 99.—RAY-FUNGUS, WITH ONE OF THE RAYS MORE PROJECTING AND BRANCHING. (*Ponfick.*)

The threads radiate from the centre, and their clubbed extremities impart to the fungus the characteristic ray-like appearance. Sometimes but one of these bulbs is connected with a thread; at other times there may be several. In some specimens one of the rays projects far beyond the others and terminates by several bulbous ends, as is shown in Fig. 99. In man the actinomyces occurs as a small, globular mass, commonly about the size of a millet-seed, usually of a pale-yellow color, but at times white, brown, green, or speckled, the color being influenced by age and the consecutive pathological conditions by which it may be surrounded. In man the clubbed bodies are often absent, and the growth then consists of the radiating filaments alone. The rays, when immersed in water or in a weak solution of chloride of sodium, become enormously swollen and lose their shape; while they effectually resist the action of acids, ether, and chloroform.

Staining.—For staining the actinomyces, Weigert uses Wedl's orseille; Marchand, eosin; Dunker and Magnussen, cochineal-red; Moosbrügger, hæmatoxylon-alum; and Partsch, in section-staining, has had the best results with Gram's method. Recently, Babés has made beautiful dry preparations by using a 2-per-cent. solution of safranin in aniline-oil, followed by treatment with iodide of potassium.

O. Israel has found that a solution of orcein in acetic acid stains the rays a Bordeaux-red, while the filaments, if decolorization is not carried too far, present a blue tinge. Baranski uses picro-carmine for staining fresh preparations of actinomyces bovis. A small amount of the contents of a yellow nodule, or pus from the part, is spread in a thin layer on a cover-glass and dried in the air. The cover is then passed three times through the flame of an alcohol-lamp, care being taken not to overheat the preparation. It is then floated in the picro-carmine solution, or a few drops of the staining fluid are placed on the cover. The whole process of staining is completed in two or three minutes. The cover is then carefully washed by agitating it in distilled water and alcohol, and examined in water and glycerin. The fungus takes a yellow color, while the remaining structure appears red.

Cultivation Experiments.—It has been found extremely difficult to cultivate the actinomyces outside of the body, probably on account of the usual culture media not being well adapted for its growth. The first successful experiments were made in 1886 by Boström, of Giessen, upon plates of coagulated blood-serum and agar-agar, the fungus attaining its maturity in five or six days, when it presented the typical structure of actinomycosis as found in man. O. Israel cultivated the fungus successfully upon coagulated blood-serum. Upon this medium the culture grows very slowly and the fungus often undergoes calcification. Israel made the observation that water, glycerin, blood-serum, and weak saline solutions seriously impair the vitality of the fungus, and he maintained that the effect of these agents on the actinomyces explains the failure of previous culture and inoculation experiments. If evaporation is prevented, a thin, velvety layer forms on the surface of the blood-serum in about eight weeks, in the vicinity of which, not before the expiration of fourteen days, cell-nodules appear more in a downward direction than on the sides of the inoculation streak. From the tenth to the fourteenth day numerous spores are produced and a thick wall of club-shaped mycelia in typical centrifugal arrangement.

At a meeting of the Medical Society of Berlin, March 5, 1890, M. Wolff made a communication in which he described culture experiments with actinomyces which he made jointly with James Israel. He announced that they had succeeded in cultivating the fungus in and upon coagulated albumen of egg and agar-agar. The material used was taken from a case of retromaxillary actinomycosis immediately after the abscess was incised. With the yellow granules stab and streak inoculations were made, using agar-agar as a soil. It was found that the actinomyces is not a purely anaërobic fungus, as it grew upon the surface as well as in the depth of the culture soil. The agar culture appeared first as transparent little drops, which, by confluence, made an opaque, white mass. Under the microscope the culture was seen to be composed of short, thick rods, with an admixture of other elements. The egg cultures, on the other hand, were made up of short, thick rods besides a mass of threads, some of them twisted in the shape of a corkscrew, presenting an intricate net-work of threads. With these cultures successful inoculation experiments were made.

Inoculation Experiments.—In 1883, James Israel succeeded in producing the disease artificially in a rabbit by introducing a fragment of actinomycotic tissue into the peritoneal cavity. Somewhat later, Ponfick made successful inoculation experiments in calves by implantation of infected granulation tissue under the skin into the abdominal cavity or directly into veins. Rotter experimented on calves, pigs, dogs, guinea-pigs, and rabbits, and in only one instance, a rabbit, did he succeed in reproducing the disease. In this case a piece of granulation tissue the size of a bean was inserted into the peritoneal cavity, and the animal, having manifested no symptoms of disease, was killed six months after the inoculation. On opening the abdominal cavity, about twenty nodules, varying in size from the head of a pin to a hazel-nut, were found distributed over a considerable surface around the graft, each of them showing the typical histological structure of actinomycosis. The transplanted piece of tissue was found perfectly encapsulated in one of the nodules the size of a bean. As the fungus was found in all the nodules, it is only reasonable to conclude that the disease spread from the original focus by migration of some of the new fungi, which, at their respective points of localization, established independent centres of infection and tissue proliferation. While the actinomyces in the new nodules presented a perfect structure, and could be readily stained, the transplanted fungus in the graft had lost its structure, and could no longer be stained. The first successful inoculation experiments with pure cultures were made by Wolff and James Israel. Three rabbits were inoculated by injecting a pure culture into the peritoneal cavity. The post-mortem showed numerous nodules upon the parietal peritoneum, the omentum, and between the intestinal coils. The nodules varied in size from the head of a pin to that of a hazel-nut, and each of them was surrounded by a fibrous capsule. The interior of each nodule was composed of a yellow mass the consistence of tallow. Typical actinomyces were found imbedded in masses of round cells in a state of fatty degeneration.

SOURCES OF INFECTION.

As regards the history of the parasite outside the body, as yet only a few facts are known. It is found in pig-meat, and is peculiarly susceptible to outside influences. Virchow found the fungus as a small, calcareous concretion in the muscle-fibres of the pig, and considered their flesh highly dangerous food unless well cooked. As the actinomyces found in man and beast resemble each other morphologically and in their effect on the tissues, as well as in their reaction to chemical substances, it is evident that the etiology of the disease is similar in both. The fungus has never been found outside of the body. Israel is of the opinion that both man and animals are infected from the same source, such as vegetables or water. Jensen traced an epidemic in Seeland to the eating of rye grown on land recently reclaimed from the sea; and Johne discovered a fungus closely resembling actinomyces in grains of rye stuck in the tonsils of pigs. That the ears of barley or rye are sometimes the carriers of the fungus is well illustrated by the case reported by Soltmann. The patient was a boy who had swallowed an awn of barley. The foreign body lodged in the pharynx, where it gave rise to difficulty in deglutition ; afterward it perforated the pharyngeal wall,—an accident attended by hæmorrhage,—and later an actinomycotic phlegmon developed; it spread rapidly, and finally opened below the scapula. Through this opening the foreign body was extracted. Piana examined the tongue of a cow suffering from a circumscribed actinomycosis of this organ, in which the disease could be traced to a similar origin,—perforation of the tissues and infection by a sharp beard of an ear of barley. Actinomycosis has as yet only been found amongst herbivorous and omnivorous animals, including man, and the frequent location of the primary swelling in the mouth seems to indicate that the fungus gains entrance with food.

PATHOLOGY AND MORBID ANATOMY.

As to the manner in which the fungus exerts its pathogenic action much yet remains to be ascertained. The most striking effect is the transformation of mature connective tissue into embryonal or granulation tissue. The fungus possesses no pyogenic properties. It gives rise in the tissues to a low grade of chronic inflammation, and becomes imbedded in the specific product of tissue proliferation,—granulation tissue.

The product of inflammation around each fungus consists of granulation tissue, which, under the microscope, might be easily mistaken for tubercle or sarcoma tissue. At first the cells are round ; at a later stage of the inflammation epithelioid and giant cells are formed immediately around the fungus. As the disease is almost always attended by suppuration at some time during its course, it has been customary to ascribe to the actinomyces pyogenic properties. Israel has always held that the actinomyces is a pus-producing fungus, in opposition to Ponfick and other pathologists, who claim that when suppuration takes place it is the result of a secondary infection with pus-microbes. As cases of actinomycosis have been recorded in which the disease remained stationary in the granulation stage, for an indefinite period of time, without suppuration taking place, and pus-microbes have been cultivated from the pus of actinomycotic abscesses, it appears more than probable that suppuration occurred independently of the presence of the fungus, and was produced by the specific action of pus-microbes on the granulation tissue. Firket asserts that the actinomyces does not appear to produce coagulation necrosis, but, from a study of the earliest-formed colonies, he finds that the first effect of the fungus is to induce cellular hyperplasia. It is as if the tissue elements resented the intrusion of the parasite, which, however, mostly gains the upper hand; so that the result is the formation of granulation tissue and, later, abscesses that characterize the disease. Suppuration takes place earliest when the disease occupies a location where secondary infection with pus-microbes is most liable to occur. As a rule, it may be stated that, the earlier suppuration takes place, the more rapid is the spread of the disease and the graver the prognosis; while the absence of suppuration indicates comparative benignity, and points in the direction of a more chronic form of the affection.

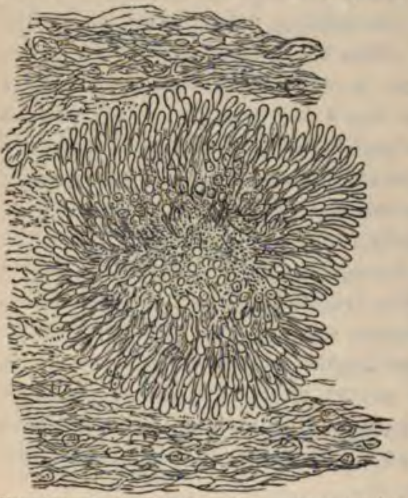

FIG. 100.—ACTINOMYCES. SECTION FROM ACTINOMYCOTIC SWELLING. × 300. (*Fluegge.*)

The localized chronic form of actinomycosis resembles, in its clinical features and its anatomical locations, more closely sarcoma than any other affection, and is most frequently mistaken for this form of malignant growth. In such cases it would be difficult, if not impossible, in the absence of the specific fungus, to make a differential diagnosis between it and round-celled sarcoma, even by a most careful microscopical examination, as the histological structure of both is almost identical.

CLINICAL VARIETIES.

If infection take place by fully-developed actinomyces, it can only do so by the fungus gaining entrance into the tissues through some loss of continuity in the cutaneous or mucous surface; any other method of ingress is impossible on account of the large size of the fungus. In the cases in which no such primary infection-atrium could be found, it must be taken for granted that the local lesion had healed between the time infection took place and the first manifestations of the disease, or that infection was caused by the entrance of spores, which, from their smaller size, could possibly find their way into the tissues through intact mucous surfaces. In reference to the primary localization of the disease, Moosbrügger gives the following statistics: In 29 cases the lower jaw, mouth, and throat were affected; in 9, the upper jaw and cheek; in 1, the tongue; in 2, the region of the œsophagus; in 11, the intestines; in 14, the bronchial tract and the lungs; in 7 the point of entrance could not be ascertained. Infection may take place through any abraded surface brought in contact with the specific cause, and for clinical purposes the cases may be divided into the following three groups: 1. Cutaneous surface. 2. Alimentary canal. 3. Respiratory tract.

1. Cutaneous Surface.—A number of well-authenticated cases of primary actinomycosis of the skin have been placed on record. Partsch describes a case of actinomycosis developing in the scar left after extirpation of the breast. The patient was a man aged 60 years. In June, 1884, his left breast was removed for an ulcerating carcinoma. As the wound did not heal by primary union, and the process of cicatrization was very slow, a number of small skin-grafts from a perfectly healthy young man were transplanted. The wound was practically healed in September. Two months later the cicatrix ulcerated and an abscess discharged itself. Actinomyces were found in the pus. The parts were excised, and the progress of the disease was apparently arrested. No explanation could be made as to how the infection occurred. Hochenegg reported a case of primary actinomycosis of the skin in the left submaxillary region. He attributed the disease to an invasion of the fungus through a small atheroma.

In Kaposi's case, when the disease was first noticed, it appeared as a red spot, the size of a florin, on the left pectoral muscle, which gradually increased to the size of a walnut and then gradually flattened down and disappeared. Meanwhile, fresh spots and lumps appeared, some as large as a pigeon's egg. Eleven years after the beginning of the disease, a swelling as large as an apple appeared over the spine of the sixth vertebra, which gradually extended forward and, a year later, formed a large tumor behind the right axilla. A year later this swelling had diminished in size to that of a pigeon's egg, and then again increased in size. Ulceration set in, exposing a fungous, bleeding surface. At this time the entire trunk, but not the limbs, was covered with nodules, spots, and stripes. The infiltration was located in the corium. This case is remarkable for the chronicity of the disease, the multiple points of regional infection, and the limitation of secondary infection with pus-microbes to a few isolated nodules.

At the meeting of the German Society of Surgeons, in 1889, Leser reported 3 cases of primary actinomycosis of the skin that had come under his own observation in the course of a single year. In his remarks on this subject he placed special stress on the manner in which the disease extends. In the periphery of the primary lesion he found numerous minute nodules, later becoming the seat of destructive changes, resembling in this respect the clinical features of tuberculosis of the skin. The extension of the disease in the direction of the deep tissues takes place by the formation of passages corresponding to the size of a lead-pencil; these are filled with yellowish-gray or reddish-gray granulations, which attack and destroy tissues, irrespective of their anatomical structure. The lymphatic glands were always found intact.

2. Alimentary Canal.—The frequency with which the disease affects the mouth and jaws of cattle is explained by the occurrence of numerous points of injury caused by masticating rough food, that furnishes the necessary infection-atrium through which the fungus invades the tissues.

Teeth.—In man infection takes place frequently through carious teeth, and through abrasions in the gums and mucous membrane of the mouth. Israel found the fungus in the cavities of carious teeth, and Partsch detected in the same locality almost pure cultures without any manifestation of disease except chronic peri-odontitis. The fungus occurs here often side by side with leptothrix.

Tongue.—Hochenegg saw a case of actinomycosis of the tongue caused by an infected carious tooth. The swelling was the size of a cherry, located near the apex of the organ. The affection had existed for two months. The growth was excised, and on examination was found to consist of granulation tissue, with a central yellow mass the size of a millet-seed. Besides this case only 3 cases of actinomycosis of the tongue are on record,—1 primary, 1 secondary to disease of the jaw, and 1 metastatic.

Jaws.—That carious teeth furnish a frequent infection-atrium in maxillary actinomycosis is well known, and in many instances the disease in its early stages has been mistaken for an ordinary dental affection, and patients have often sought relief at the hands of a dentist. The lower jaw is most frequently affected, the growth being connected with the bone or situated close to it, or it has already extended to the submental or submaxillary region. The disease often pursues a chronic course, closely simulating periosteal sarcoma, until it reaches the loose tissues of the neck, when rapid extension takes place, in a downward direction, along the subcutaneous connective tissue and the intermuscular septa. Israel refers to a case in which the actinomycotic swelling in the submaxillary region extended, in five months (August to December), to the level of the thyroid cartilage. When the disease is primarily located in the upper jaw, which, however, occurs only in exceptional cases, it tends to invade rapidly the adjacent soft parts, and even to implicate the base of the skull and the brain. The prognosis is always more serious when the disease affects the upper than the lower jaw, as the tendency here to invade the deep structure is much greater. Two cases of actinomycosis in man have come under my observation, and as both of them originated in the mouth, and represent, from a prognostic point of view, two distinct classes, I will describe them briefly.

The first patient was a man 30 years of age, German by birth, and a soda-water manufacturer by occupation. His business required him to make frequent trips into the country by team. He had no recollection of having come in contact with cattle suffering from "swelled head" or "lumpy jaw." During the winter of 1886 he suffered from what he supposed was an ordinary cold; the right side of the lower jaw was swollen and painful. As one of the molar teeth showed evidences of decay and had become loose, it was extracted. The pain and swelling, however, did not improve, and the attending physician extracted all of the molar teeth of the lower jaw on that side. At this time a fungous mass commenced to appear over the surface of the edentulous bone. The cheek on the affected side was also greatly swollen. The patient was admitted into the Milwaukee Hospital about six months after the first symptoms had appeared. At this time the lower jaw, in the mouth, presented a fungous mass extending from the angle of the bone to the first bicuspid; the swelling extended as far as the tonsil. The cheek was enormously swollen from the angle of the mouth to the lower margin of the parotid gland. The skin over the swollen part presented a pale, glossy appearance, and the superficial veins were considerably dilated. Around the margin of the swelling no distinct border-line could be felt, the infiltrated parts fading gradually into the healthy surrounding tissues. Free suppuration from the surface of the fungous granulations, and a number of [illegible] had discharged themselves into the cavity of the mouth. As some doubt existed as to the character of the inflammation, careful and repeated examinations were made of the pus removed from the small abscess-cavities, and on several occasions fragments of actinomyces were found. The discovery of the specific cause of the inflammation cleared up the diagnosis and furnished an urgent indication for operative treatment. An incision was made along the lower border of the jaw from just below the articulation to near the symphysis, and, after arresting all hæmorrhage, it was carried into the cavity of the mouth. The alveolar processes of the jaw were affected, and were removed with chisel and cutting-forceps. Wherever the periosteum showed signs of infiltration it was carefully scraped away, and finally the whole bone surface was thoroughly cauterized. The infiltrated soft tissues were dissected out with knife and scissors; the disease was found to have extended as far as the tonsil. The bottom of the wound was iodoformized and packed with iodoform gauze, while the external wound was sutured. The entire external wound healed by primary union, and the cavity in the mouth closed slowly by granulation. The patient's general health continued to improve rapidly, until six weeks after the operation, when the neck below the scar became swollen, followed in a short time by the formation of abscesses reaching from the angle of the jaw to the clavicle, and posteriorly as far as the spine of the scapula. Numerous openings were made and efficient drainage established, but suppuration continued unabated, and the patient became extremely emaciated. The suppurative inflammation extended, and four months after the first operation the patient died; the symptoms during the last days of life pointed to a hypostatic pneumonia. Actinomyces were continuously found in the pus during the entire course of the disease. I believe that the recurrence of the disease was due to imperfect removal of infected tissues in the posterior and lower portion of the pharynx.

The second case came under my care during the summer of 1887. The patient was a young man, employed on a farm. About five months before he was admitted into the Milwaukee Hospital he had a number of teeth extracted from the right upper jaw, under the belief that the teeth, some of which were decayed, were the cause of the pain and swelling in that region. The physician in attendance diagnosed sarcoma of the upper jaw, and sent the case to me for operation. On my first examination, I found a swelling involving the right side of the face, extending from the zygomatic arch to near the lower border of the lower jar, involving the deep tissues, and connected with the alveolar processes of the posterior portion of the upper jaw. The swelling was firm and without well-defined margins. No evidences of suppuration. The history of the case, and particularly the location, extent, and physical properties of the swelling, led me to the opinion that it was the result of actinomycotic infection. All infected tissue was thoroughly excised through a large external incision, the jaw-bone scraped and cauterized. The entire thickness of the cheek, with the exception of the skin and superficial fascia, appeared to be transformed into granulation tissue. In the granulations numerous minute yellowish-gray bodies were found, which, under the microscope, showed the typical structure of the ray-fungus. The mycelia were not so bulbous as we find them pictured in the books, but the distal extremity appeared to be surrounded by dust-like bodies, presenting the appearance of a small brush. These minute granules I regarded as spores. In the first case, in which suppuration had taken place, I never succeeded in finding the actinomyces perfect and complete; in the second case the granulation tissue had not been destroyed by suppuration, and the fungus was found in a perfect condition and in a state of fructification. These cases present a striking contrast, both in regard to the local condition and the ultimate termination. In the first case secondary infection with pus-microbes had already taken place, and the phlegmonous inflammation that followed this occurrence prepared the tissues again for the diffusion of the actinomycotic process; while in the second case the inflammatory process had not passed beyond the granulating stage, and the boundary-line between healthy and diseased tissue was also more distinctly marked,—a most important factor in the operative treatment. The first patient died from recurrence of the disease in the vicinity of the operation wound and its extension to the neck and chest; while in the second case the wound healed, and the patient has remained in perfect health since.

3. Intestinal Canal.—In primary intestinal actinomycosis the disease is caused by ingress of the fungus with food or water, and its implantation upon the mucous surface. At the point of implantation the fungus multiplies, and by its growth invades the submucous tissue, which becomes the seat of active tissue proliferation. Arrest and implantation of the actinomyces are determined by antecedent pathological changes. Chiari has given an excellent account of the pathological condition found in a case of intestinal actinomycosis that came under his observation. The patient was a man 36 years of age, who during life presented, as the most prominent clinical feature, progressive marasmus. At the necropsy chronic tuberculosis in the apices of the lungs and a few tubercular ulcerations in the lower portion of the ileum were found. The large intestine presented a very remarkable appearance, the mucous membrane of which, except the cæcum and ascending colon, was covered with whitish deposits, forming round and oblong patches, some of them 1 cubic centimetre in diameter and 5 millimetres in thickness. In some of these patches could be seen minute yellowish-brown and yellowish-green granules. The patches were firmly adherent, and when removed left a loss of substance in the mucous membrane. The mucous membrane throughout was in a state of catarrhal inflammation. On microscopical examination the granules proved to be actinomyces. The mycelium had penetrated into the tubular glands and showed calcified, club-shaped conidia. The calcification of the club-shaped extremities had undoubtedly prevented deeper penetration of the fungus. Hochenegg presented a case of actinomycosis to the Medical Society in Vienna in a man 43 years of age, who had sustained an injury of the abdomen nine months previously, and had since that time noticed a painful swelling at the seat of injury. In the region of the umbilicus a fistulous opening formed, which continued to discharge a thin secretion, in which actinomyces were constantly found. The patient was very much emaciated and many of the teeth carious. There was no swelling about the jaws or neck. Examination of the organs of the chest and the sputum revealed no additional diagnostic information. The author expressed the opinion that the inflammatory swelling caused by the contusion furnished the necessary conditions for the localization of actinomyces from the intestinal canal.

Zemann reports 5 cases of actinomycosis of the abdomen. In 4 of them the disease commenced with sharp, lancinating pains in the abdomen, and during their course presented the clinical picture of chronic peritonitis. Swellings could be found in one or more places in the anterior abdominal wall, and the abscesses were either incised or opened spontaneously, and in 3 cases they communicated with the intestinal canal. The first case was a woman, 30 years of age, who had a fistulous opening in the anterior abdominal wall which communicated with a swelling in the left parametrium. The patient stated that this swelling appeared soon after her last childbed. A constant discharge of yellowish-red pus was maintained, in which, under the microscope, numerous actinomyces could be seen. The patient died of exhaustion, and at the post-mortem chronic para- and peri- metritis were found, with extensive pus-cavities that communicated with the rectum and bladder. The second case occurred in a person 18 years of age, who, during life, had suffered from a large abscess in the abdominal cavity, under the right lobe of the liver, which communicated with the intestinal canal, and had led to numerous fistulous openings in the anterior abdominal wall.

At the necropsy a loop of the ileum was found perforated and in communication with the abscess-cavity. The pus contained numerous actinomyces. In the third case the diagnosis was made post-mortem by the discovery of actinomyces in the pus. The disease was located in the lower portion of the ileum and cæcum, where it had caused suppuration and numerous adhesions. A most remarkable and interesting history is connected with the fourth case. A robust, well-nourished woman, 40 years of age, was attacked quite suddenly with pain in the stomach, high temperature, diarrhœa, and vomiting, followed by cerebral symptoms and death. At the necropsy the right Fallopian tube was found transformed into a large abscess, both extremities of the tube closed, and walls of sac lined with granulations containing actinomyces. The fifth patient was 50 years of age, and had suffered for a long time from lancinating pain in the abdomen; a fistulous opening formed in the umbilical region and discharged a thin, yellowish-green pus. The post-mortem showed actinomycosis of the peritoneum, small intestine, left ovary, and liver; large abscess among the intestinal coils; perforation of small intestine and bladder. In the upper part of the small intestine small pigmented cicatrices were found. In all of the above cases the microscopical examination revealed the presence of actinomyces in the granulation tissue as well as in the pus of the abscess-cavities. In a case of intestinal actinomycosis reported by Langhans, the disease started evidently from the appendix vermiformis, 4 centimetres in length, the end of which appeared as if transversely cut in an abscess-cavity the size of a walnut. The abscess was on the right side of the bladder, and so deep in the pelvis that during life it could not be located. The abscess pursued a chronic course, and the walls were well defined; no signs of chronic or acute peritonitis. Furthermore, the mucous membrane of the appendix was studded with cicatrices, and presented a slate color. The principal seat of the actinomycotic process was in the liver. In a second case reported by the same author the clinical course of the disease resembled perityphlitic abscess. The necropsy showed perforation of the cæcum and ascending colon. No cicatrices in the mucous membrane or surrounding tissues. In all probability, the perforations occurred from without inward.

Luening and Hamm have recently reported, with interesting details, a case of primary actinomycosis of the colon with metastatic deposits in the liver. The patient was a man 28 years of age, who, in 1880, suffered from an acute abdominal affection, which at the time was diagnosed as typhlitis. Four years later a second attack occurred, attended by symptoms of intestinal obstruction. Patient was very ill for eight days, when the symptoms of obstruction subsided, and he made a slow recovery. During the year 1887 he had a third attack, attended by high fever and absolute constipation for eight to ten days. During the month of December of the same year he had another but less severe attack, and at this time a hard swelling made its appearance in the right side of the abdomen. From this time until he was admitted into the hospital, April 5, 1888, he was confined to bed. The patient was at this time greatly emaciated, with a temperature of from 38.4° C. to 39.8° C. Swelling the size of a fist in the right side of the abdomen, half-way between umbilicus and anterior superior spine of the ileum. Externally this swelling presented redness and œdema. Fluctuation indistinct. Deep palpation showed that the swelling extended to right hypochondrium; abdomen not tympanitic. Swelling painful and tender, pain extending to spermatic cord and testicle on same side. A few days later abscess was incised, and nearly a quart of brownish pus, having a fæcal odor, escaped. Digital exploration revealed an irregular cavity, whose walls at some points were plainly lined with intestinal coils. Disinfection and drainage. As the symptoms did not improve materially, the abscess-cavity was again scraped out and disinfected four weeks later. After the second operation it was noticed that the pus contained yellow granules, which, under the microscope, were shown to be actinomyces. The abscess was incised a third time, but the patient kept losing ground, and died October 9th. The autopsy revealed primary actinomycosis of the ascending colon, with multiple fistulous perforations. A metastatic actinomycotic abscess of the liver had perforated into the hepatic vein, resulting in multiple metastases in the lungs. The cases of intestinal actinomycosis reported above warrant the opinion that the mucous membrane of the intestinal canal is frequently the seat of primary localization of the actinomyces, thus corroborating the statements of Johne in reference to this disease in animals.

BRONCHIAL TUBES AND LUNGS.

If an actinomyces should be inhaled with the inspired air, and should become implanted upon the bronchial mucous membrane, and find favorable conditions for its growth, the granule will become surrounded by new cells derived from the pre-existing epithelial cells, and thus become the centre of a minute granuloma.

By multiplication of the actinomyces new nodules are produced, around each of which the pre-existing tissue is transformed into embryonal tissue, which in time is destroyed, resulting in suppuration and loss of tissue. Israel reported a case of actinomycotic abscess of the lung caused by the entrance of an infected tooth into the air-passages. In this instance the fungus was conveyed into the bronchial tube with the carious tooth, and the infected foreign body became the centre of the specific inflammation.

Cases of primary actinomycosis of the lungs, however, have been observed where no such direct carrier of the contagium could be found, and in which infection must have occurred by the direct inhalation of the fungus or its spores with the inspired air. Szenásy found, in the case of the wife of a butcher, who had suffered for nine years from severe pain in the right side of the chest, latterly attended by a severe cough, in the right mammary region, a fluctuating swelling, the size of a hen's egg, covered with normal skin. On the outer side of this swelling, in the intercostal space between the third and fourth ribs, another swelling existed, double in size and elongated in shape, and with indistinct margins. This latter swelling has been noticed for nine years, and was tender to the touch. Auscultation over the fourth and fifth intercostal spaces on the healthy side revealed bronchial breathing and diffuse bronchial râles. Temperature, 38.4° C. (101.1° F.). The urine contained a trace of albumen. By aspiration 150 cubic centimetres of thick, yellow pus were removed, and contained colonies of actinomyces. Actinomyces were also found in the sputum. The patient had carious teeth, but no signs of actinomycosis could be detected in the mouth.

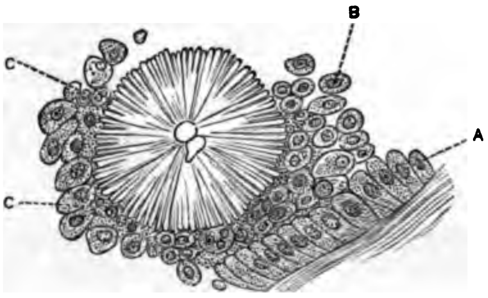

FIG. 101.—ACTINOMYCES FROM LUNG OF COW. FUNGUS IN THE CENTRE OF INFLAMMATORY PRODUCT. × 350. (*Marchand.*)

A, normal epithelial cells of bronchus attached to connective tissue; B, large epithelioid cells; C, leucocytes.

Canali relates the clinical history of a girl, 15 years of age, who had suffered for eight years from a cough, attended by a scanty, fetid expectoration. Inspection and percussion yielded only negative results. Auscultatory symptoms pointed to a diffuse catarrh. Under the microscope the sputum was seen to contain pus-corpuscles, epithelial cells, and numerous actinomyces. No primary source of infection could be found in the mouth, pharynx, or nose.

Moosbrügger interprets the mechanism of the ingress of actinomyces by assuming that the fungus enters the bronchial tubes during inspiration, and becomes at first deposited upon the mucous membrane, where its presence and growth cause a destruction of the epithelial cells, when it reaches the submucous and peri-bronchial tissues, in which a nodule of granulation tissue is produced that by pressure induces degenerative changes and gradual destruction of the bronchial wall for further infection. He believes that the peri-bronchial lymphatic vessels and glands take an active part in the local diffusion of the process, as they furnish an avenue for the dissemination of the fungus or its spores. He claims the existence of an actinomycotic lymphangitis, but confesses that he has never seen the fungus inside of lymphatic vessels. As soon as the fungus reaches the pulmonary tissues, it gives rise to parenchymatous inflammation, whose first product is always granulation tissue, which, at a later stage, and under the influence of a secondary infection with pus-microbes, undergoes transformation into pus-corpuscles and the formation of abscesses.

ACTINOMYCOSIS OF BRAIN.

Quite recently, Böllinger placed on record the first case of primary actinomycosis of the brain. The patient was 26 years of age. The *intra vitam* diagnosis was tumor of the brain; the most prominent symptoms were severe headache, paralysis of left abducens, congestion of optic papilla, and momentary unconsciousness. The swelling in the brain, found on autopsy, presented the characteristic features of a cystomyxoma in the third ventricle; all of the ventricles were found considerably dilated. The swelling contained numerous colonies of actinomyces in all possible stages of development. The tendency to suppuration of the tissues, usually found in all cases of actinomycosis in man, was entirely absent in this case. This case, if any, appears to be one of cryptogenetic infection, as the fungus or spores must have entered somewhere through the cutaneous or mucous surface without producing the disease at the primary *portio invasionis*, and, localizing in the brain by embolism, resulted in primary actinomycosis in this organ.

Keller (*Brit. Med. Journal*, March 29, 1890) reported, this year, a case of metastatic actinomycosis of the brain in which a correct diagnosis was made during life. The patient was a middle-aged woman, who suffered from pleurisy, and six months thereafter abscess developed over the cartilages of the sixth and eleventh ribs, in the pus of which actinomyces were found. Two years later increasing paresis of left arm developed, followed by convulsions, confined at first to the arm, then becoming general, and at times identical with cortical epilepsy. Diagnosis of actinomycosis affecting the motor area was made; operation was suggested and declined. The paresis extended to left lower extremity and left side of face; later, convulsions, headache, vomiting, and loss of consciousness, soon deepening into coma. Burger then obtained consent to operate. The patient was moribund, and required no anæsthetic. He exposed the right ascending parietal convolution, incised the dura mater and the discolored brain-surface, and removed 2 ounces of thin, greenish pus, in which were found actinomyces in great abundance. When the pus was evacuated, she recovered from the deep coma, and, while still on the operating-table, called for water. On the following day consciousness returned, and on the eighth the facial paralysis disappeared. In two months the wound had healed and the paralytic lesions improved, but there remained some paresis of left arm, with contraction of the fingers. In less than one year there was a recurrence of the symptoms, and Burger re-opened the brain-abscess, followed by the escape of a considerable quantity of pus. No material improvement followed, and the patient died a few days thereafter.

At the post-mortem, the middle third of the right frontal and parietal convolutions was occupied by a large mass of newly-formed tissue, protruding over the surface and reaching into the substance of the brain for one inch. Underneath it, deeply buried in the white substance, an unopened, encapsulated abscess, the size of a nutmeg, was discovered.

SYMPTOMS AND DIAGNOSIS.

Actinomycosis is an inflammatory disease that clinically is noted for its chronicity. The specific product, composed of granulated tissue, is abundant, and the swelling, often of considerable size, resembles more a tumor than an inflammatory swelling. The extension of the morbid process takes place by effusion of the actinomyces *in loco*, in preference along the loose connective-tissue spaces, each fungus constituting a nucleus for a nodule of granulation tissue. By confluence of many such nodules the inflammatory swelling often attains a very large size, and when suppuration occurs in the interior the further history is that of chronic abscess. Regional dissemination of the infective process never takes place through the lymphatic glands. When the lymphatic structures become implicated, it is an indication that secondary infection has taken place. In exceptional cases the disease pursues quite a rapid course, and may then be mistaken for an acute phlegmonous inflammation, osteomyelitis, or, when diffused over a large surface of the body, for syphilis. A good illustration of the former class is furnished by the case reported by Kapper. A soldier, 22 years of age, became suddenly ill with febrile symptoms and a rapidly-increasing swelling of the lower jaw. An early incision was made and liberated a large quantity of pus, which, on microscopical examination, was found to contain actinomyces. It is interesting to note that in this case the various teeth from where the infection had evidently taken place contained threads of leptothrix and actinomyces.

At a meeting of y, about two years ago,

O. Israel gave an accurate description of the post-mortem appearances of a case of diffuse actinomycosis. The patient, a woman 44 years of age, had been treated for syphilis in one of the surgical clinics. The heart contained a number of minute abscesses containing the fungus in large numbers. A large abscess between the diaphragm, stomach, and spleen contained thick pus of a greenish color,—an unusual occurrence in cases of actinomycosis,—but no actinomyces. The spleen was the seat of large and numerous minute abscesses, and the liver and kidneys also contained small abscesses, and in all of them actinomyces were found. Israel claims that this case affords a good illustration of his view that the actinomyces, as regards its effect on the tissues, occupies a position half-way between the bacillus of tuberculosis, which produces only granulation tissue, and the pus-microbes, which produce pus. It was impossible in this case, as in so many others in which multiple deposits have been found, to locate with accuracy the primary seat of infection. The teeth were perfect and the whole digestive tract showed no evidence of disease. Metastasis in actinomycosis takes place in the same manner as in pyæmia and malignant tumors. At the primary seat of infection the fungus or its spores gain entrance through a defective vein-wall into the general circulation, and, at the point of arrest in a distant capillary vessel, establish an independent centre of infection, with all the attributes of the primary infection. General infection is of rare occurrence in actinomycosis, as this disease is noted for its tendency to extend locally, where it often results in external regional dissemination and destruction of tissue. Actinomycosis resembles, in its clinical behavior, very closely the malignant tumors, in that it will invade every tissue with which it comes in contact, irrespective of its anatomical structure. Primary localization is very apt to occur in the connective tissue, and in preference it extends along this structure; but periosteum, bone, muscles, tendons, cartilage,—in fact, all of the tissues of the body,—succumb to the fungus as quickly as they become infected.

In actinomycosis of the jaws and the vertebræ we often find extensive destruction of bone, with large abscesses communicating with the primary lesion. Before suppuration takes place the actinomycotic swelling is quite firm on pressure, and, if the disease extend rapidly, it is surrounded by a diffuse œdema. Pain and tenderness are usually never severe, and often almost wanting. Redness appears as soon as the infection has extended to the skin. Suppuration usually develops in consequence of direct infection with pus-microbes through some minute surface defect in the swelling. As soon as suppuration sets in, the swelling not only increases rapidly in size, but regional diffusion is hastened by the breaking down of the granulation tissue that before held the fungi fixed in their respective localities. The same tendency to migration of an actinomycotic abscess is observed as in tubercular abscess. The characteristic feature of actinomycotic pus is the presence of minute, macroscopical, yellowish granules; the actinomyces, on careful inspection, can almost always be discovered. If these granules are placed under the microscope their characteristic structure will at once become apparent.

In cases of actinomycosis of any of the internal organs, attended by suppuration and discharge of pus through some one of the outlets of the body, the diagnosis will usually depend almost exclusively upon the detection of the fungus in the discharges. Microscopical examination of the sputum and fæcal discharges, in cases of suspected actinomycosis of the lungs or the intestines, is the only positive means of making a differential diagnosis between these affections and pulmonary and intestinal tuberculosis. Actinomycosis of the skin, mouth, tongue, and jaws might be mistaken for sarcoma, carcinoma, tuberculosis, and syphilis. As, with the exception of carcinoma, all of these affections present under the microscope a histological structure that it would be often difficult to identify microscopically, the differential diagnosis by means of the microscope must rest on the detection of the ray-fungus imbedded in the granulation tissue. Sarcoma does not suppurate or break down as early as the actinomycotic or tubercular swelling. Carcinoma primarily starts in the epiblast or hypoblast, and, even during the earliest period of the growth, there is no difficulty in demonstrating an intimate relationship between the skin or mucous membrane and the tumor encroaching upon the mesoblast. In actinomycosis, tissue proliferation takes place around each fungus in the mesoblast, and the skin or mucous membrane is infected and destroyed from within outward. In tuberculosis, regional infection almost always occurs through the medium of the lymphatic vessels and glands, while these structures are seldom or never invaded in actinomycosis. In the absence of microscopical proof of the nature of the lesion, it may become necessary to resort to a therapeutic test in differentiating between syphilis and actinomycosis. Large doses of potassic iodide, administered four times a day, will have a decided effect in reducing the size of a gumma in the course of two or three weeks, while no such result will be obtained if the lesion is of an actinomycotic nature.

PROGNOSIS.

Actinomycosis is a more dangerous affection than tuberculosis. While a spontaneous cure not infrequently takes place in the latter, we have no proof that actinomycosis ever terminates in such a satisfactory manner without the surgeon's aid. Actinomycosis of the internal organs proves fatal almost [illegible] on account of the inaccessibility of the disease to radical surgical treatment. In such cases numerous fistulous openings form, discharging profuse quantities of pus, and the patient dies in from one to two or three years from exhaustion or amyloid degeneration of the internal organs. If the disease is located in external parts, local extension often takes place very slowly until suppuration sets in, when the actinomycotic abscess migrates from place to place, attacking all the tissues that come in its way, and life is finally destroyed by pyæmia, sepsis, or exhaustion. The prognosis is always favorable when the disease is recognized early, and when it is located in parts accessible to a radical operation. As metastasis is of rare occurrence in actinomycosis, complete removal of the primary focus is followed by a permanent cure.

TREATMENT.

General treatment in actinomycosis is of no avail, and all local measures, short of complete removal of the infected tissues, result in more harm than good, as they often give rise to secondary infection with pus-microbes, which always aggravates the local conditions and hastens a fatal termination. In cases where a radical operation is out of question on account of the extent of the disease or the importance of organs involved in the process, parenchymatous injections of a 2-per-cent. solution of boric acid, a 1-to-1000 solution of corrosive sublimate, or a 1-to-1500 solution of nitrate of silver might be tried; but, on the whole, such injections have little influence in arresting the local extension of the disease. The surgical treatment of actinomycosis, before suppuration has occurred, consists in the excision of the infected tissues in all cases where such a procedure is practicable. The incision should be carried some distance, at least ½ to 1 inch, from the visible granulations, with a view of removing not only the inflammatory tissue, but also the minute invisible foci in its immediate vicinity. If, after the excision, suspicious tissue is found in the wound, this should be removed by a careful dissection with forceps, knife, and scissors, or destroyed by using the actual cautery. Acids and other chemical caustics should not be relied upon in destroying the infected tissues. An actinomycotic abscess should be treated on the same principles as a tubercular abscess. The abscess-cavity is freely exposed by laying open the fistulous openings, and the granulation tissue is removed with a sharp spoon. Undermined skin is cut away with scissors. If the disease has extended to bone, this is also thoroughly scraped, and it is a good plan, after the cavity has been thoroughly irrigated and dried, to cauterize the whole surface with the actual cautery. Such wounds should not be sutured, but packed with iodoform gauze in order to keep the infected area readily accessible to inspection, so as to enable the surgeon at each dressing to recognize a local recurrence. Should this occur, the same means are to be repeated in eliminating the infected tissues. As soon as the wound is covered with healthy granulations it may be closed by secondary suturing, or, if this cannot be done on account of too great loss of skin-tissue, the defect is covered with large skin-grafts according to Thiersch's method. Repeated scraping operations will often succeed in finally eradicating the disease, provided the infected parts are accessible to vigorous curetting and the application of the actual cautery.

CHAPTER XXIII.

ANTHRAX.

SYNONYMS: Contagious carbuncle; charbon; Milzbrand; malignant pustule; wool-sorters' disease. The mycology of anthrax is better understood than that of any other microbic disease. The bacillus of anthrax is the largest of the known pathogenic microbes, and ever since it was discovered it has been a favorite subject of investigation in every laboratory and by every bacteriologist.

HISTORY.

As a disease among animals, anthrax has been known since the earliest records of history. The contagiousness of this disease has been recognized since the beginning of the eighteenth century. During the first part of the present century it was described as a blood disease. Heusinger, in his classical work, " Die Milzbrand Krankheiten der Thiere und des Menschen " (Erlangen, 1850), declared anthrax to be a malarial neurosis. In the year 1855 Pollender published his discoveries, which inaugurated a new era in the study of anthrax. As early as 1849 he discovered, in the blood of cattle suffering from anthrax, a mass of innumerable, fine, rod-like bodies, which appeared to be of a vegetable nature and resembled vibriones. Branell found the same rods in the blood of men, horses, and sheep which had died of anthrax. He also detected the same bodies during life in the blood of the diseased animals. Delafond regarded this parasite as a variety of leptothrix. In 1863 appeared the work of Davaine, wherein he pronounced these rods to be bacteria, and later he called them *bacteridia*. He believed them to be the essential cause of anthrax, as the disease could not be found in blood that did not contain them. Through the labors of Pasteur, Koch, Nægeli, Böllinger, and others, the bacterium found so constantly in the blood and tissues of anthracic animals finally found a permanent place as the bacillus anthracis among the schizomycetes.

The first reliable and positive accounts of the disease in man we owe to Fournier, Montfils, Thomassin, and Chabert, who published their description of the disease between the years 1769 and 1780. Fournier first distinguished the spontaneous and the communicated carbuncle of man. The primary existence of anthrax in man was asserted by Bayle in 1800 and by Davy la Chevrie in 1807.

DESCRIPTION OF THE BACILLUS OF ANTHRAX.

Non-motile rods, 5 to 10 micro-millimetres long and 1 to 1.25 micro-millimetres broad, and threads made up of rods and cocci.

The rods, as a rule, are straight; only when they grow to a considerable length and meet with resistance they become slightly curved. The rods and threads are round, and, with their threads truncated at right angles, appear as though they had been cut off obliquely. The interior, as long as fission does not proceed, is perfectly homogeneous, and absorbs aniline dyes very readily and uniformly. The development of spores in long, undivided threads, as we find them in fluid culture media, takes place at regular intervals, where we find them as bright, oval spots that become more and more apparent, marking the direction of the rods. Upon solid culture media the development of spores is preceded by transverse segmentation of the rods. The cell-membrane of each section finally becomes the membrane of the spore, each pole of the spore presenting a small mass of protoplasm that can be stained.

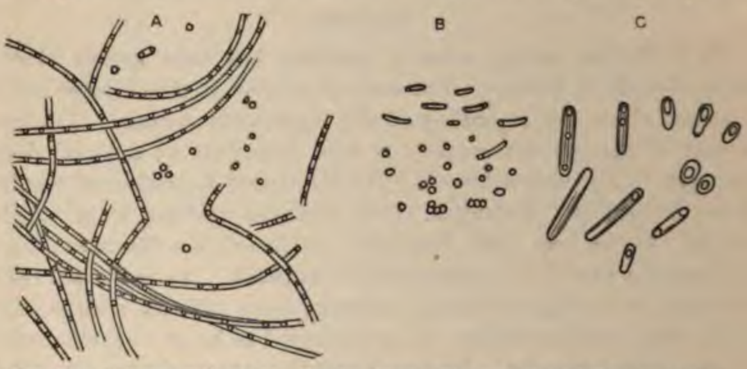

FIG. 102.—ANTHRAX BACILLI. SPORE FORMATION AND SPORE GERMINATION. (*Koch.*)

A. From the spleen of a mouse after twenty-four hours' cultivation in aqueous humor. Spores arranged in rods like a string of pearls. × 650. B. Germination of spores. × 650. C. The same greatly magnified. × 1650.

(a) **Staining.**—Cover-glass preparations of fluid specimens can be stained with a watery solution of any of the aniline dyes. They can be rapidly stained with a drop of fuchsin or gentian-violet, but more satisfactorily by floating the cover-glass for twenty-four hours. The preparations are dried and mounted in Canada balsam. The spores are not stained by the ordinary methods. Tissue-sections containing bacilli are best stained by Gram's method, and after-stained with eosin or picrocarminate of ammonium. By double staining the rods are seen to consist of a hyaline sheath with protoplasmic contents.

(b) **Cultivation.**—The bacillus of anthrax grows luxuriantly in different fluid and solid nutrient media. Bouillon and aqueous humor of the eye furnish an excellent soil, but for inoculation purposes the cultures are now generally grown upon solid nutrient media.

Gelatin.—If a nutrient medium containing from 5 to 8 per cent. of gelatin is inoculated, a whitish line develops in the track of the needle-puncture, and from it fine filaments spread out on the sides.

In a more solid nutrient gelatin the growth appears only as a thick, white thread. The culture liquefies the gelatin, and the growth subsides as a white, flocculent mass.

Plate Cultures.—Cultures upon a sloping surface of solid nutrient agar-agar or gelatin form a viscous, snow-white plaque.

Without access of air the culture does not grow, the bacilli being aërobic.

Potato.—Inoculation of sterilized potato yields a very characteristic growth. The deep chamber containing the potato is placed in the incubator, and in about thirty-six or forty-eight hours a creamy, very faintly yellowish layer forms over the inoculated surface, with, usually, a peculiar translucent edge. On removing the cover of the damp chamber, a strong, penetrating odor of sour milk is emitted.

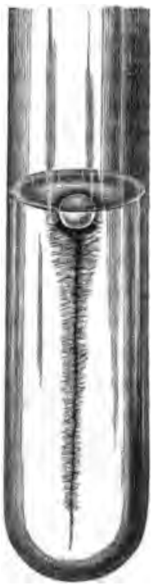

FIG. 103.—STAB CULTURE OF ANTHRAX BACILLI IN GELATIN, GROWN AT ROOM-TEMPERATURE (16° TO 18° C.). FOUR DAYS OLD. NATURAL SIZE.
(*Baumgarten.*)

MULTIPLICATION OF ANTHRAX BACILLI IN THE LIVING BODY AND THE SOIL.

In the body of living animals the bacilli multiply exclusively by segmentation, and never produce spores. Spores are produced only in dead nutrient media, and under certain conditions only, among which a proper temperature is the most important factor. The limits of the temperature vary between 12 to 18° C. and 43° C.; at a temperature of less than 12° C. growth of the rods and spore production no longer take place. Pasteur's assertion that bacilli and spores in the cadavers of buried animals are active when brought to the surface by earth-worms is improbable. The disease, according to Koch, is spread among animals by germinating spores which attach themselves to plants and grass in swamps and along river-banks, and which, when taken in with the food, become the cause of intestinal anthrax.

Schrakamp and Friedrich are of the opinion that bacilli can multiply in the superficial layer of the soil, while Kitt maintains that fructification of the bacilli takes place in the manure deposited in pastures.

INOCULATION EXPERIMENTS.

In order to cause death of animals by inoculation with the bacillus of anthrax, a pure culture or anthracic blood must be injected into the subcutaneous tissue or into the circulation, or the virus may be transmitted by inhalation or by feeding. Goats, hedgehogs, mice, sparrows, cows, horses, guinea-pigs, and sheep can be readily infected. Rats are less susceptible. Pigs, dogs, cats, white rats, and Algerian sheep are immune. Frogs and fish have been rendered susceptible to anthracic infection by raising the temperature of the water in which they lived. Koch produced the disease artificially in rabbits and mice by injecting a drop of anthracic blood, with the result of producing death usually within twenty-four hours. After death sections taken from different organs, stained in methyl-violet with carbonate of potash, were examined under the microscope, and the bacillus was found in great abundance in all of them. When magnified fifty diameters such preparations present, at the first glance, an appearance as if a blue coloring material had been injected into the vessels. Each intestinal villus is permeated by an exceedingly delicate blue net-work; in the mucous membrane of the stomach all the capillaries surrounding the gastric glands are stained blue; in the ciliary processes each projection is injected, and a spiral vessel stained of a dark-blue color leads from

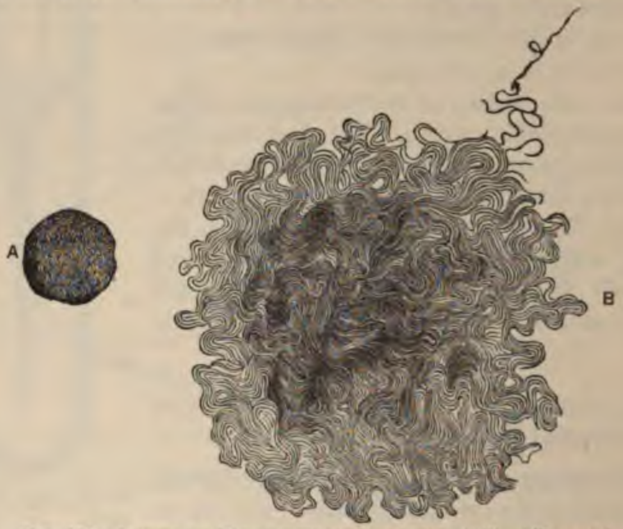

FIG. 104.—ANTHRAX COLONY UPON GELATIN. ×80. (*Fluegge.*)
A, after twenty-four hours: B, after forty-eight hours.

thence to the iris and breaks up into a fine, blue net-work, with loops directed toward the edge of the iris. The liver and lungs and the glandular structures, such as the pancreas and salivary glands, are completely permeated by the same blue, vascular net-work. Indeed, there is no organ which is not more or less injected with the blue mass. It is, however, very striking that this injection is only present in the capillary vessels. All the larger vessels, even the arteries and veins of an intestinal villus, are either not at all stained or have but a light-blue streak in their interior, and that only here and there. When magnified 250 times one can see that the blue capillary net-work is composed of numerous delicate rods, and when a power of 700 diameters is used it is found that the apparent injection is nothing more or less than the bacillus anthracis, stained dark-blue, and present in incredible numbers in the whole capillary system.

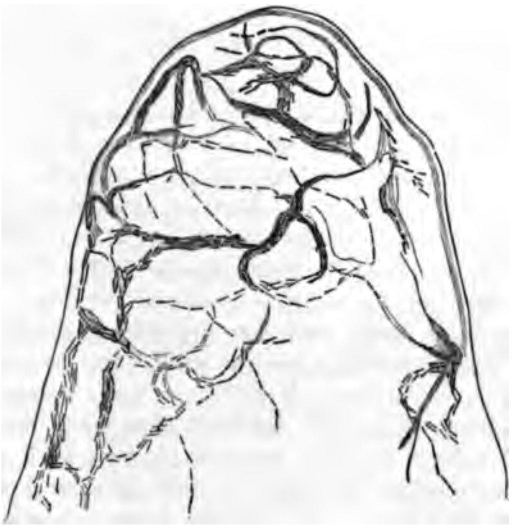

FIG. 105.—INTESTINAL VILLUS OF ANTHRACIC RABBIT. THE BACILLI IN CAPILLARY VESSELS ALONE STAINED. × 250. (*Koch.*)*

In the other vessels, especially in the larger ones, often only a single bacillus may be met with at long intervals, or they may be quite absent.

The distribution of the bacillus in the capillaries is not, however, quite uniform. There are fewer in the brain, in the skin, in the capillaries of the muscle, and in the tongue than elsewhere; on the other hand, in the liver, lungs, kidneys, spleen, intestines, and stomach they are always present in enormous numbers. In the capillaries themselves the bacilli accumulate in largest numbers at the point most distant from the nearest afferent artery and the efferent vein,—that is, at points where the blood-current is slowest. Where the bacilli are present in greatest abundance it not unfrequently happens that the capillaries become torn, and blood with the contained bacilli is extravasated. This occurs most frequently in the glomeruli. Many of these burst, and the bacilli pass into the uriniferous tubules. In mice the spleen is more especially the seat of the bacilli; then come the lungs, and, last of all, the kidneys. Frisch inoculated the cornea in animals and produced a keratitis, caused by the bacilli, which multiplied with great rapidity, local dissemination taking place through the corneal spaces.

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* Copied from "Traumatic Infective Diseases," by permission of the New Sydenham Society, London.

INFECTION IN MAN.

An intact skin furnishes ample protection against infection with bacilli or spores, but the slightest abrasion may become the necessary infection-atrium for either method of infection. Infection may occur through a healthy mucous membrane, either with bacilli or spores. As the anthrax bacillus is a non-motile parasite, penetration of the epithelial lining can only occur by local growth of the bacillus. Spores are such minute structures that they can reach the circulation through a healthy mucous membrane in the same manner and by means of the same agencies as we have found necessary for the transportation of other minute foreign parasites from a mucous surface into the circulation. In man infection frequently takes place through a small wound or abrasion in persons handling the infected products of anthracic animals, such as wool, hair, and hides. In other instances, insects, such as mosquitoes and flies, that have fed on the blood of living anthracic animals or the dead tissues of animals that died of the disease, may become disease carriers. The sting of such an infected insect may communicate the disease with the same degree of certainty as an intentional inoculation with a drop of anthracic blood or a minute quantity of a pure culture.

INTENSIFICATION OF VIRUS.

While it is known that some chemical substances exert an attenuating influence on the virulence of the anthrax bacillus, it has also been found that an attenuated virus will again become more virulent by adding certain substances. It must, therefore, be taken for granted that the chemical composition in which the bacillus is suspended influences, in one way or the other, its virulence. It has been found, for instance, that the addition of a minute quantity of lactic acid to a fluid containing the bacillus in an attenuated form greatly intensifies its virulence within a very short time. Thus, Arloing, Cornevin, and Thomas found that the pathogenic power of a fluid containing these bacilli, to which $\frac{1}{600}$ part of lactic acid had been added, and the mixture allowed to stand for twenty-four hours, was increased twofold; if, then, a little water, containing a very easily fermentescible sugar, is added to the mixture, and another twenty-four hours allowed to elapse, the virulence attains its maximum, and frogs inoculated with this virus die in from twelve to fifteen hours; whereas, when inoculated with ordinary virus, they live from forty to fifty hours. Kitt has repeated and confirmed these experiments.

ATTENUATION OF VIRUS AND PROPHYLACTIC INOCULATIONS.

By cultivating the bacillus of anthrax in neutralized bouillon at 42° to 43° C. (107.6° to 109.4° F.), for about twenty days, the infecting power is weakened, and animals inoculated with it are protected against the disease. A still greater degree of immunity is obtained by inoculating a second time with material that has been less weakened. Animals thus treated are then protected against the most virulent form of anthrax, but only for a time. A temperature of 55° C. (131° F.), or treatment with 1- to 5-per-cent. solution of carbolic acid, deprives the bacilli of their virulence. The virulence of the bacillus is also altered by passing it through different species of animals. Woolbridge secured immunity against anthrax in animals by cultivating the bacillus in an alkaline solution at a temperature of 37° C. (98.6° F.) for two days. At this time the fluid was filtered, and a small quantity of the filtrate injected into the subcutaneous tissue of rabbits; these rabbits remained well, and subsequently resisted injection of most virulent anthracic blood.

Hankin, under the guidance of Koch, at the Hygienic Institute of Berlin, isolated an albuminose from anthrax cultures, which, when injected into rabbits and mice in small quantities, rendered these animals immune against the most virulent cultures. The albuminose was prepared from the cultures by precipitation with absolute alcohol; the precipitate was well washed in this liquid to free it from ptomaines,—since it is known that all such substances are soluble in alcohol. After the addition of alcohol it was filtered off and dried, then re-dissolved, and filtered through Chamberland's filter. Four rabbits were inoculated with virulent anthrax spores, and 3 of them received an injection of albuminose into the ear-vein at the same time; the latter recovered, while the remaining animal not thus protected died, in about forty-eight hours, of anthrax. In another experiment, 10 mice were each injected with the millionth part of their body-weight of anthrax albuminose and with active vaccine at the same time. Of these 3 died after 108 to 116 hours; the others recovered. Three others had only the two-millionth part of their body-weight of anthrax albuminose and active culture. Two of them survived. Four control mice were inoculated, and all died of anthrax. He has come to the conclusion that when a large dose of albuminose is injected into an animal the entrance of anthrax bacilli into the system is aided, and when a small dose is administered immunity is acquired against its poisonous properties, protecting the animal against subsequent inoculations with active cultures. Prophylactic inoculations of sheep with mitigated virus is carried on upon an extensive scale in France by Pasteur and his pupils, and recent statistics bearing upon their value in protecting the animals against anthrax have shown them effective in preventing the spread of the disease in infected districts.

CLINICAL VARIETIES OF ANTHRAX.

Primary bronchial and pulmonary anthrax, caused by the inhalation of dust containing bacilli or spores, and primary anthrax of the intestines, caused by eating anthracic meat or by drinking water infected with spores, are diseases that are occasionally met with in man; but, as these affections belong to the physician and not to the surgeon, the student should consult any of the modern text-books on the practice of medicine to become familiar with their symptomatology.

Buchner has studied experimentally the entrance of the anthrax bacillus through the intact mucous membrane of the bronchial tubes. The bacillus and spores were administered by inhalations, in the shape of dry powder, and suspended in steam. On examining the bronchial mucous membrane at different stages under the microscope, it was seen that the spores were transformed in a very short time into bacilli, and that the latter, by their growth, pushed themselves between the cells and into the capillary vessels. It was observed that the greater the pulmonary irritation, the more the passage of the microbes was retarded. The entrance of the bacilli from the surface of the mucous membrane into the capillary vessels was seen to depend on an active process.

Secondary anthracic bronchitis, pneumonia, and enteritis are met with in almost all cases of localized anthrax followed by secondary general infection. Primary intestinal anthrax in man was studied by Wahl, Recklinghausen, Buhl, Wagner, Böllinger, Leube, and Fränkel, and all of these authors succeeded in demonstrating the presence of the essential microbic cause in the inflamed mucous membrane. When the microbe enters the body through the mucous membrane of the gastro-intestinal canal with the food or drink, it gives rise to a primary anthrax of the intestinal canal, that again may become general by metastatic dissemination through the systemic circulation. Localization upon the mucous surface first takes place upon the most prominent part of the valvulæ conniventes on the mesenteric side of the bowel, and from here the infection spreads over the entire surface. Vierhoff has collected 41 cases of anthrax intestinalis, the total number found reported up to 1885. The author himself observed 2 cases of secondary intestinal anthrax in the hospital at Riga. Cases of secondary intestinal anthrax—that is, localization of the bacillus of anthrax in the mucous membrane of the intestinal canal after external infection—were known to the older authors, while observations of primary localization in the digestive tract date only from the middle of the last century. As soon as general infection has taken place, the diffusion throughout the capillary system is the same as has been described under the head of Inoculation Experiments. The forms of anthrax that concern the surgeon most are those which result from infection of the external surface by the introduction of the bacilli or spores through a small wound, abrasion, or the sting of an infected insect. The favorite location for the development and growth of the anthrax bacillus in man and beast is in the connective tissue; it is, therefore, immaterial in what manner the microbe reaches this tissue, as localization here marks the beginning of the disease. The clinical forms vary according to the location of the disease, its extent, and the intensity of the infection. Most all authors follow Böllinger's classification, according to which all cases are brought under one of the following varieties: 1. *Anthrax acutissimus*, or *apoplectiformis*. 2. *Acutis*. 3. *Subacutis*.

The primary location of the disease is in accordance with the manner in which infection has taken place. W. Koch states that in animals and man the bacillus can enter the organism through one of the following routes: (*a*) through the skin; (*b*) gastro-intestinal canal; (*c*) respiratory passages.

Anthrax of the External Surface.—Infection of the sub-epidermal connective tissue can only occur through a defect in the epidermis; hence, every anthrax of the external surface corresponds in its location with an infection-atrium, through which the essential microbic cause has entered the connective tissue. The bacillus of anthrax, when brought in contact with living tissue susceptible to its pathogenic action, causes an acute inflammation characterized by grave alterations of the capillary wall and rapid exudation. The microbe first multiplies at the primary point of invasion, and, if it does not meet with sufficient tissue resistance, it enters the blood-vessels and causes general infection, which always proves fatal. Infection occurs most frequently in exposed parts of the bod cases of anthrax in man, collected by Slessarewskji, times on the face, 21 times on the neck, and sseau relates that in Paris 20 persons were attacked with anthrax in ten years, and in all of them the source of infection could be traced to horse-hair imported from South America. The pathologico-anatomical conditions vary according to the primary seat of invasion, the structure of the organ, and seat of the disease. The first tissue changes are observed at the point of inoculation. From a prognostic and pathological point of view, external anthrax can be divided into two distinct varieties: 1. *Anthrax pustule.* 2. *Anthrax œdema.*

1. Anthrax Pustule.—This is the so-called malignant pustule. It is usually met with in parts not covered by clothing, as the fingers, hands, and face. This form of the disease is determined by the anatomical structure of the part affected, which must be dense and vascular. The pustule begins as a small, red point that resembles the bite of a flea, in the middle of which a small vesicle appears, which, at first, contains a transparent serum, and, later, becomes sanguineous. The patient complains of an itching, burning sensation. The skin around the centre of the pustule is at first slightly raised by the inflammatory infiltration underneath it. Within twenty-four or forty-eight hours the size of the infiltrated area is as large as a nickel, and the inflamed part presents all the evidences of a very acute circumscribed inflammation. The swelling is now painful, tender on pressure, and exceedingly firm to the touch. The centre, previously occupied by a vesicle, is of a brownish-red or blackish-gray color, and presents indications of approaching gangrene. The epidermis exfoliates, exposing a necrosed area the size of a pea to a silver half-dollar. The dead tissue remains firmly connected with the surrounding indurated parts, until it becomes gradually detached in the course of the suppurative inflammation, which ensues sooner or later. After separation of the slough, spontaneous healing may take place, always leaving a depressed scar. In this form of anthrax general infection seldom occurs, as the infection remains local, the early and abundant inflammatory exudation forming an impermeable wall around the infected zone, beyond which the bacilli cannot escape. General infection, however, in such cases occasionally takes place where a vein becomes implicated in the process, and general infection is not prevented by the formation of a plastic thrombus on the proximal side of the intra-venous culture. The acuteness of the inflammation, and probably, also, the direct necrotic effect of the ptomaines of the bacilli, invariably result in necrosis of the central portion of the pustule, which is the most characteristic pathological and clinical feature of this form of anthrax.

2. Anthrax Œdema.—This form of anthrax follows infection, if the tissues around the infection-atrium are freely supplied with loose connective tissue and the blood-supply to the part is scanty,—conditions which are present about the eyelids, neck, and forearm. Anthrax in these localities appears as a flat infiltration without well-defined borders, and with little or no discoloration of the skin. From the infiltrated tissues a rapidly-spreading œdema extends in all directions. This form of anthrax is attended by greater danger of general infection than anthrax pustule, as the bacilli are less effectually walled in by the inflammatory product. Vesication, exfoliation of cuticle, and gangrene may also take place, and in milder cases a spontaneous cure is possible. As long as the infection remains local general symptoms are absent, but as soon as general infection has occurred the symptoms point to progressive septicæmia.

PATHOLOGY AND MORBID ANATOMY.

If the tissues of a primary anthrax of the external surface are examined under the microscope, all the appearances of an acute non-suppurative inflammation are shown. The specific effect of the bacillus on the tissues results in serious alteration of the capillary vessels, which gives rise to an abundant inflammatory exudation. In malignant pustule, or anthrax pustule, the para-vascular and connective-tissue spaces become completely blocked with leucocytes in a remarkably short time, and necrosis of the central portion of the inflammatory product is a constant result of the acute ischæmia and the speedy coagulation necrosis thus produced. Anthracic inflammation never terminates in suppuration unless secondary infection with pus-microbes takes place. The local œdema in the œdematous variety, at the point of infection, is caused by vascular disturbances due to the presence of the bacilli within the blood-vessels and the interstitial inflammatory exudation caused by their presence. In fatal cases the necropsy reveals the same changes in different organs as Koch has described in his experiments on rabbits. The capillary vessels in every part of the body will be found completely or partially blocked with bacilli, but the number of microbes is always greatest in the most vascular organs, as the spleen, liver, and kidneys.

The bacilli, as in mice-septicæmia, will be found in the capillary vessels arranged in the direction of the blood-current, and most numerous where the flow of blood is most impeded, as at points of intersection. General infection always takes place through blood-vessels. The internal organs are found enlarged and exceedingly vascular from engorgement caused by the capillary obstruction. Minute extravasations are found in different organs where the bacilli are most numerous, resulting in complete destruction of the capillary wall and rhexis. The secondary intestinal affection most frequently assumes the form of inflammatory hæmorrhagic infiltration, more seldom that of hæmorrhagic catarrh; ulcerations the size of a split pea to 2 inches in diameter are frequently present, the remaining portion of the mucous membrane showing well-marked evidences of acute inflammation, great vascularity, and infiltration. Mesenteric glands are swollen and contain numerous bacilli. The bronchial and intestinal mucous membranes show all the appearances of recent inflammatory changes, great vascularity, slight thickening, and here and there minute extravasations. In some cases the meninges of the brain show well-marked lesions that account for the cerebral symptoms during life. Pathologists have often failed in locating the immediate cause of death in fatal cases of anthrax, and various theories have been advanced at different times to determine this point.

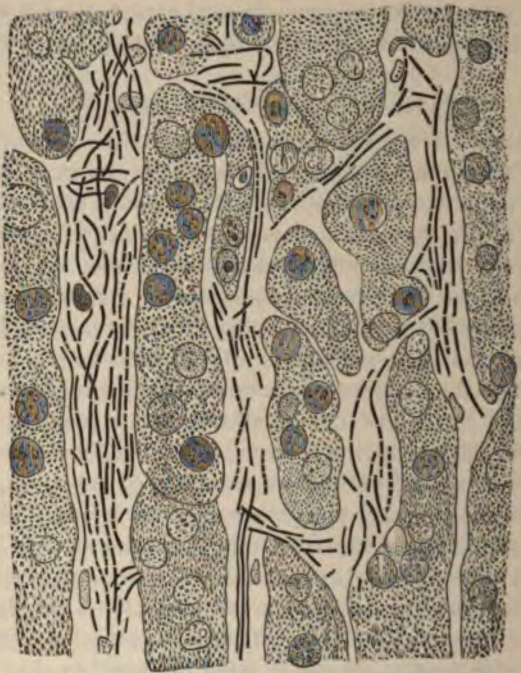

FIG. 106.—ANTHRAX. SECTION FROM LIVER. × 700. (*Fluegge.*)

In the most virulent form, the anthrax acutissimus, Böllinger believes that the rapid growth of the bacillus in the blood brings about a sudden diminution of oxygen and a surplus of carbonic acid, and that death takes place by a slow process of asphyxia. Against this theory it can be maintained that, in the blood of animals that have died of the acutest form of the disease, comparatively few bacilli are found; and, further, that in the experiments made by Nencki, on the blood of rabbits that had died of this form of anthrax, it was found as capable of oxygenation as the blood of healthy animals. The theory that death results from purely mechanical causes, due to the presence of bacilli in great abundance in the blood-vessels, is likewise not tenable, because no such fatal degree of obstruction in the capillary circulation has been found at the post-mortem examinations. As a third hypothesis, Böllinger advanced that the bacillus may generate a chemical poison that may cause death by intoxication. In reference to the last-mentioned cause, Hoffa calls attention to the following three possibilities:—

1. The bacilli of anthrax are in themselves poisonous, and the increase in their number increases the quantity of the poison in the same ratio. Against this supposition the results of the experiments made by Hoffa himself furnish the most conclusive proof. Of a pure culture of anthrax bacilli he injected a large quantity directly into the jugular veins of rabbits. The animals thus infected showed no symptoms of acute intoxication, but died in the same manner as animals infected in the usual way.

2. The bacilli of anthrax produce a poison capable of causing fermentation in the blood; this poison is soluble in the blood. The fact that filtered blood of animals that had died of anthrax did not produce toxic symptoms when injected into healthy animals speaks against this argument.

3. The bacillus of anthrax separates toxic substances from complex combinations in the organism. This last explanation appears, from analogy of the views that are now entertained of bacteria and ptomaines, to be the most plausible, and he made an effort to produce such substances outside of the animal body upon artificial culture media. For this purpose he cultivated the bacillus with the greatest precautions upon sterilized meat kept for several weeks in an incubator at 37° C. (98.6° F.). The chemical product thus obtained he attenuated according to the methods advised by Stass-Otto, Brieger, and after the more recent method of Fischer.

By the methods of Stass-Otto and Fischer he succeeded in producing a substance that possessed an alkaline reaction, and produced toxic effects in animals. A strictly-pure article and an accurate chemical description of it could not be obtained, on account of the smallness of the quantity produced. The substance produced by Stass-Otto's method was used in experimenting on frogs, mice, guinea-pigs, and rabbits; both of them produced symptoms of intoxication. After a short period of intoxication, with increased action of the heart and accelerated respiration, the animals became somnolent; respirations deep, slow, and irregular, assisted by the action of all accessory muscles of respiration; pupils dilated, temperature normal, diarrhœa, fæces bloody; speedy death. At the necropsy the heart was found contracted, the blood was of a dark color, and ecchymosis of the pericardium and peritoneum existed. There were no micro-organisms in the blood. The pathological conditions described here are an accurate duplication of the post-mortem description in fatal cases of anthrax. The same author succeeded subsequently in isolating, by a complicated process, a toxic substance from the bodies of anthracic rabbits with the formula $C_3H_6N_2$, which he called *anthracin*, besides a small quantity of methylguanidin. To the former substance he attributes the toxic symptoms in cases of anthrax. Injected subcutaneously in rabbits, it produced first restlessness, rapid pulse, and accelerated respiration, followed by somnolence, deeper and slower respiration, diarrhœa, asphyictic symptoms, convulsions, and death. This substance is closely allied to *kreatin*, and contains 23 per cent. of nitrogen. These experiments leave but little doubt that the fatal termination in cases of anthrax is caused by the action of toxic ptomaines formed in the body in consequence of the action of the bacilli upon certain as yet unknown combinations in the organism.

DIFFERENTIAL DIAGNOSIS.

Anthrax must be distinguished from other forms of acute circumscribed inflammation, notably from furuncle and carbuncle. A furuncle is conical from the beginning, and the summit is transformed into a small slough. A carbuncle is nothing more nor less than a multiple furuncle, and is produced by the same microbic cause. Anthrax develops from a single centre, and the infiltration proceeds from this point in all directions. Necrosis is preceded by vesication, and the black, necrosed tissue is fully exposed after exfoliation of the epidermis. The œdematous form of anthrax might be mistaken for erysipelas or acute phlegmonous inflammation. Anthrax œdema is usually not attended by much discoloration of the skin, and there is no such distinct and abrupt line of limitation as in erysipelas. Phlegmonous inflammation, when advanced to the extent where it may resemble anthrax œdema, has gone on to the stage of suppuration. The differential diagnosis between malignant œdema and anthrax can only be made by searching for the primary cause by the use of the microscope. A positive differential diagnosis between suppurative lesions and anthrax can be made in the course of one or two days by inoculation experiments. If a rabbit or mouse is infected with a drop of anthracic blood or serum taken from the centre of the inflammatory product, death from anthrax will follow within two days; while the same amount of fluid taken from a suppurative depot will produce no effect, or, at most, only a circumscribed abscess. As the anthrax bacillus can be readily stained and identified under the microscope, a positive differential diagnosis between these affections can always be made by the use of the microscope.

PROGNOSIS.

The location of the disease, the character of the tissues primarily affected, and the general condition of the patient greatly influence the prognosis in cases of anthrax. The prognosis is most favorable in young, healthy individuals suffering from anthracic pustule, as in such instances the general strength of the patient and the active tissue proliferation at the seat of infection are well calculated to prevent general infection; while, in persons debilitated from any cause affected with the œdematous variety, general infection is very liable to follow. An anthrax œdema of the hand or arm is a less serious condition than a similar affection of the face or neck. As a general rule, it may be stated that, the firmer and more circumscribed the local lesion, the more favorable the prognosis, and, *vice versâ*, the more extensive the area of infection and the more diffuse the œdema, the greater the danger to life from general infection. The occurrence of general infection may be recognized without difficulty by the general symptoms which indicate the existence of progressive septic infection. The bacillus of anthrax multiplies with great rapidity after its entrance into the circulation, and the anthracin, which produces the septic symptoms, is elaborated in amounts proportionate to the number of bacilli in the body. Fever, cough, rapid respiration, feeble and rapid pulse, diarrhœa, and delirium are some of the symptoms indicating that the disease has become general. All hope of recovery must be abandoned as soon as general infection has occurred; death from progressive infection and intoxication will be certain to take place, in spite of the most heroic local and general treatment.

TREATMENT.

The surgical treatment of anthrax must be directed toward the elimination or neutralization of the primary microbic cause. As within the living body the reproduction of the primary cause takes place exclusively by segmentation of the bacilli, any germicidal agents that inhibit or destroy the pathogenic property of the bacilli will be found useful in the local treatment of anthrax. It has been found experimentally that a 5-per-cent. solution of carbolic acid will arrest the growth of anthrax cultures, and clinical experience has demonstrated that the same solution, when brought in contact with the infected tissues by parenchymatous injections, has a decided influence in arresting further extension of the infection.

Lande reports 2 cases of malignant anthrax saved by parenchymatous injections of carbolic acid. In the first case, a man aged 27, the upper lip was the seat of the disease; in the second, a woman aged 65, the anthrax occupied the region below the scapula. Both patients were very ill, low delirium and other symptoms of toxæmia being present. The injections were made into the subcutaneous tissue around the pustule. The strongest solution used consisted of 15 grammes of neutral glycerin and an equal part of distilled water, in which 3 grammes of pure carbolic acid were dissolved. The injections were made at five points around the pustule, and represented a total dose of 50 centigrammes of the acid. The injections caused considerable pain, but rapid improvement followed. The solution used—10 per cent.—was stronger than any previously employed for the same purpose by Bœckel, Raimbert, and others. A 5-per-cent. solution in ordinary cases is strong enough, but in grave cases the 10-per-cent. solution must be used until improvement takes place, which should occur within forty-eight hours. The object of the parenchymatous injections should be to saturate, as far as possible, all of the infected tissues with the antiseptic for the purpose of destroying the bacilli, and, at the same time, to permeate the surrounding healthy tissue for some distance, with a view of destroying the soil for the growth of the microbes in advance of the invasion. The surface over the entire infected area should be rendered thoroughly aseptic, in order to prevent secondary infection with pus-microbes through the needle-punctures. The punctures should be made a few lines from the border of infiltration, but always toward the centre of the infected district. The injection is made gradually as the needle is withdrawn, so as to saturate the tissues for some distance along the entire length of the track of the needle. At one sitting from four to twelve injections are made, according to the size of the anthrax and the urgency of the symptoms. A compress wrung out of a 1-to-1000 solution of corrosive sublimate should be kept constantly applied. Application of an ice-bag over the antiseptic compress will assist the germicidal agents in retarding or arresting further multiplication of the bacilli in the tissues. The injections should be repeated every six hours until the disease is under control, or until it is deemed unsafe, from the quantity injected, to administer more carbolic acid for fear of causing intoxication. Excision has been objected to on the ground that the wound might become a new source of infection, and thus leave the patient in a more precarious condition, so far as general infection is concerned, than before the operation; but such is not the case if the area of infection is limited and the incisions can be made through healthy tissue. The following case affords a good illustration of the value of excision of anthrax in well-selected cases.

Kaloff, of St. Petersburg, in making experiments with anthrax on animals, accidentally infected himself, either by a needle-puncture or by handling the organs of anthracic animals. The local infection appeared on the outer side of the thumb of the left hand as a small vesicle, that soon disappeared, but gave place to circumscribed infiltration on the second day. This inflammation rapidly extended, and was surrounded with hæmorrhagic vesicles. The indurated tissues were promptly removed by excision; nevertheless, on the next day, swelling of axillary glands on same side, fever, great prostration, also diarrhœa, set in. The skin in the axillary region and side of chest was much swollen, and at different points bright-red, at others bluish-red. One of the axillary glands, the size of a hen's egg, and glands along the margins of the pectoralis major muscle were removed, and field of operation thoroughly disinfected with a 5-per-cent. solution of carbolic acid; the same solution was also thrown into the surrounding tissues with a hypodermic syringe. Cessation of fever and rapid healing of wound, followed by recovery. The diagnosis was confirmed by successful cultivations made with fragments of the excised tissue in bouillon and gelatin. Excision should always be resorted to in cases of anthrax pustule, as it fulfills the etiological indications more promptly and thoroughly than any other treatment. The incisions should be made outside of the indurated tissues, and, for the purpose of preventing traumatic dissemination of the disease, the surface, after thorough irrigation, should be brushed over with a 10-per-cent. solution of carbolic acid before the wound is sutured. This procedure will destroy any bacilli that may have become deposited upon the surface of the wound.

In the case just cited it is possible that lymphatic infection—an unusual occurrence in anthrax—developed in consequence of the entrance of bacilli into the open lymphatic vessels on the surface of the wound. Excision under strict antiseptic precautions is also justifiable in anthrax œdema, even if all of the infected tissues cannot be removed, as sterilization of the remaining portion of the infected tissues can be secured subsequently more efficiently by parenchymatous injections than if the primary focus of infection is allowed to remain as a hot-bed for progressive infection. In such cases it would be good practice to sear the whole surface of the wound with the actual cautery, for the purpose of preventing general and regional dissemination by the entrance of bacilli into the open lumina of veins and lymphatics, and also to increase the resisting capacity of the tissues to infection by exciting an active tissue proliferation. The actual cautery would prove successful in recent cases, in cutting short an attack, if resorted to before any considerable infiltration has occurred. It is said that shepherds, in districts where anthrax is endemic, destroy the vesicle with a red-hot needle as soon as it is detected, and it is seldom that the infection does not yield to this treatment. At this early stage the whole area of infection is limited, and could be most effectually destroyed with the sharp point of a Paquelin cautery. The general symptoms in severe cases of local anthrax, and after general infection has occurred, resemble the clinical aspects of septicæmia produced by other causes, and patients suffering from general primary or secondary anthrax require the same stimulating, tonic, and supporting treatment that has been laid down in the treatment of septicæmia.

CHAPTER XXIV.

GLANDERS.

SYNONYMS: Farcy; equinia; malleus humidus; Morve; Rotzkrankheit. A contagious disease characterized by multiple foci of inflammation and suppuration, and caused by infection with a specific microbe,—the *bacillus mallei*. The disease originates in the horse and occurs in men by contagion. Although glanders in man is a rare affection, it presents, from a bacteriological study, so many points of interest that it merits more than a passing notice. It is one of the infectious diseases whose microbic cause is now thoroughly understood.

BACTERIOLOGICAL HISTORY OF THE DISEASE.

That glanders in man occurred as an infection from the horse species of animals has been known for a long time. Its contagiousness among horses was asserted by Sollegsel in the seventeenth century. Rindfleisch believed that he saw vibriones in the granular contents of glanderous abscesses. Klebs detected, in cultures of pus taken from animals suffering from this disease, small rods and granules, but further cultivations and inoculations in rabbits failed. The presence of minute organisms in cases of glanders was pointed out by Christatt and Kiener in 1868, and their observations were corroborated by Bouchard, Capitan, and Charrin, who found the organisms not only in parts exposed to the air, such as nasal ulcerations and pulmonary abscesses, but also in parts not so exposed, such as the spleen, liver, and lymphatic glands. Chaveau demonstrated by his experiments that the virus of glanders was fixed to small, solid particles, as he found the sediment, which formed after dilating pus with water, active. This discovery marked an advance in the knowledge of the physical nature of the virus. Löffler and Schütz are the discoverers of the bacillus of glanders in horses. In 1882 they made a preliminary report of their researches (*Deutsche Med. Wochenschrift*, 1882, No. 52). In 1886 Löffler published his elaborate monograph on this subject ("Die Ætiologie der Rotzkrankheit," *Arbeiten aus dem Kaiserlichen Gesundheitsamte zu Berlin*, Bd. i, pp. 141-199). About the same time, O. Israel made cultures upon blood-serum from nodules of three glanderous horses, with which he produced the disease artificially in rabbits. The bacilli contained in these cultures correspond with the description of those isolated by Schütz and Löffler. Soon after Löffler's first paper appeared, Bouchard, Capitan, and Charrin published almost simultaneously the results of their researches and observations; but it appears from Löffler's second paper that none of them had been able to produce a pure culture. Kitt and Weichselbaum were the first who, by their own investigations, were able to corroborate the correctness of Löffler's discovery: the former by his observations and experiments on animals, the latter by a case of glanders in the human subject that came under his own observation.

DESCRIPTION OF BACILLUS MALLEI.

According to Löffler, the bacillus of glanders appears as a small rod, which is somewhat shorter and broader than the tubercle bacillus; its length varies but little, and corresponds to about two-thirds of the diameter of a red blood-corpuscle; the thickness varies between one-fifth and one-eighth of its length.

These bacilli are either straight or slightly curved and rounded at their ends. Usually, they are found in pairs in a parallel direction, held together by a delicate, unstained pellicle. Examined in a drop of fluid, they show active molecular movements. Spontaneous movements could not be observed by Löffler. The colorless and sometimes even somewhat dilated portions of the stained bacillus are not spores, but, as Löffler affirms, indications of commencing death. Löffler found that bacilli kept in a dry state for three months could occasionally be made to grow, but in most instances, after a few weeks, they could no longer be cultivated, which fact speaks against the existence of spores. On the other hand, in favor of the presence of endo-spores must be regarded the results obtained by Rosenthal, in Baumgarten's laboratory, with Neisser's method of staining spores, who showed that at least some of the bacilli contain spores, while in others the points which refuse staining material are undoubtedly, as Löffler claims, evidences of vacuolar degeneration.

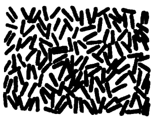

FIG. 107.—BACILLI OF GLANDERS FROM A YOUNG POTATO CULTURE. × 950. (*Baumgarten.*)

(a) **Staining.**—The method of staining the bacilli of glanders is characteristic; when the bacilli are treated by basic and aniline dyes no effect is produced.

Method of Schütz.—The sections are placed for twenty-four hours in the following mixture: Potash solution (1 in 10,000), concentrated alcohol, methylene-blue solution,—equal parts. Wash the sections in a watch-glass with water acidulated with 4 drops of acetic acid. Transfer for five minutes to 50-per-cent. alcohol, clarify in clove-oil, and mount in Canada balsam.

Löffler's Method.—Sections are immersed for a few minutes in a solution of potash (1 in 10,000), then for a few minutes in an alkaline solution of methyl-blue; after which they are decolorized with a solution of tropæolin in acetic acid, or, what is still better, in a fluid composed of 10 centimetres of distilled water, 2 drops of sulphuric acid, and 1 drop of a 5-per-cent. solution of oxalic acid.

(b) Cultivation.—When cultivated on solid sterilized blood-serum at a temperature of 38° C. (100.4° F.), the growth appears in the form of minute transparent drops on the surface, which consist exclusively of the characteristic bacilli. Cultures upon boiled potato, according to Löffler, Kitt, and Weichselbaum, form in three days a uniform amber-yellow layer, that about the sixth to the eighth day assumes a reddish hue, resembling the color of oxide of copper, which is not easily mistaken for any other culture upon the same soil. Upon this nutrient medium the bacilli were cultivated through twelve generations, and the cultures retained their activity for a year; whether the bacillus was capable of cultivation after this time is not mentioned. The temperature at which cultures could be made to grow varied from 30° to 40° C. (86° to 104° F.). The bacillus also grows in neutralized bouillon, with and without the addition of peptone. The culture first renders the fluid turbid, and, later, settles on the bottom of the vessel as a white, shining mass. Weichselbaum succeeded in growing the bacillus upon ordinary nutrient agar and gelatin. Raskina rendered these nutrient media more fertile for the growth of this microbe by the addition of chicken-natron albuminate. Kranzfeld succeeded best with Nocard and Roux's mixture,—meat-peptone, glycerin, agar-agar.

TENACITY OF BACILLUS MALLEI.

Löffler ascertained that this bacillus shows the same degree of resistance to heat and germicidal substances as other bacilli without spores. The bacillus is destroyed by exposure for ten minutes to a temperature of 55° C. (131° F.). It is also destroyed by a 3- to 5-per-cent. solution of carbolic acid in five minutes, and in two minutes in a 1-to-5000 solution of corrosive sublimate.

INOCULATION EXPERIMENTS.

Kitt enumerates the following animals as being susceptible of inoculation with the virus of glanders: Tiger, lion, cat, sheep, goats, guinea-pigs, horse, ass, rabbits, and white rat. Pigs, dogs, the common rat, ducks, and chickens possess great immunity; the inoculations at best produce only a slight local reaction. Löffler made his first experiments on guinea-pigs and the field-mouse. In the guinea-pigs he observed, three to five days after subcutaneous injection of a pure culture, an ulcer at the point of inoculation, and at the end of the first week swelling of the nearest lymphatic glands, attended by suppuration. At this stage of the disease the process often came to a stand-still and the animals recovered. In many animals the disease progressed quite rapidly to a fatal termination. Abscesses were frequently found in the testicle and the epididymis in the male, and in the breast and external genital organs of the female. The face, nasal cavity, and ankle-joint were also frequently the seat of ulcerative processes. In case the disease proved fatal, death usually occurred three or four weeks after inoculation. At the post-mortem, aside of the affections enumerated, nodules were found in the spleen, lungs, and frequently in the liver. The histological structure of a recent nodule bears a great resemblance to tubercle. The bacilli are always found more numerous in the nodules if the disease is produced artificially by inoculation. The inflammatory product is first composed almost exclusively of epithelioid cells, between which leucocytes from the periphery insinuate themselves. Giant cells are never

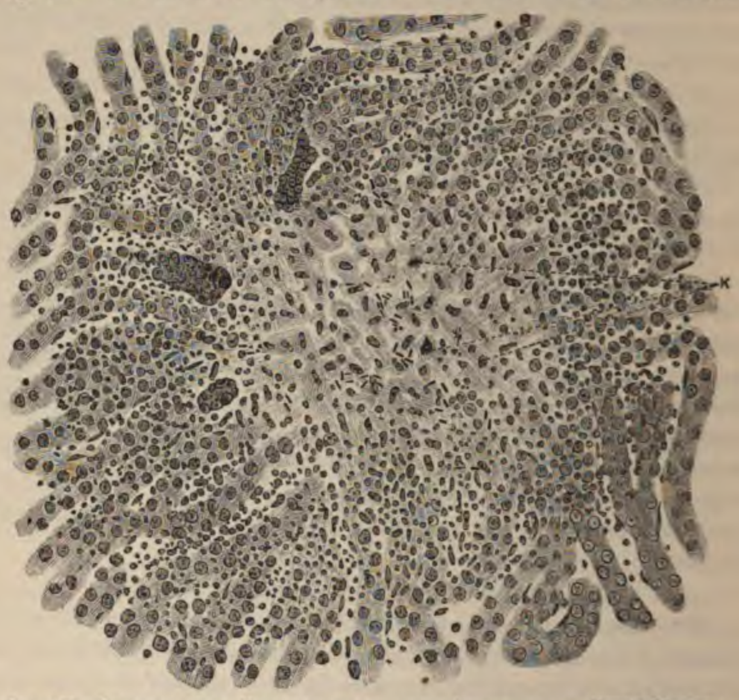

Fig. 108.—Glanderous Nodule from the Liver of a Field-Mouse. Bismarck-Brown Staining. Bacilli Stained after Löffler's Method. Bacilli Magnified and Drawn Twice this Size. ×250. (*Baumgarten.*)

K, karyokinetic figures in epithelioid cells.

found in glanderous nodules; the epithelioid cells are derivatives of connective tissue and endothelial cells; while the leucocytes escape from the inflamed capillary vessels. Baumgarten constantly observed karyokinetic figures in the epithelioid cells.

The leucocytes that enter the nodule soon show evidences of fragmentation, and are converted into pus-corpuscles. The bacilli are distributed among the cellular elements singly, in pairs, and in groups. Some of them may be seen also within the cellular elements, especially the epithelioid cells.

Field-mice proved a great deal more susceptible to the virus of glanders than guinea-pigs, as they usually died three or four days after inoculation. The necropsy in these animals showed, at the point of inoculation, an infiltration from which swollen lymphatic vessels led to the nearest lymphatic glands. In the spleen and liver, which were always found greatly enlarged, numerous small nodules could be seen, while the remaining internal organs presented a normal appearance. Glanders in guinea-pigs and field-mice presents a series of pathological changes that cannot be mistaken for any other affection. The bacilli of glanders in the different organs can be detected most readily in recent specimens. In the blood bacilli were detected only in very acute cases,—a circumstance that explains why so many inoculations with the blood of glanderous horses proved unsuccessful. The bacilli of glanders are evidently strictly tissue- and not blood- parasites.

Lundgren took a nodule from the lungs of a horse that had died of glanders, and implanted fragments of it under the skin of rabbits. The animals died about the nineteenth day after inoculation, and the necropsy revealed induration and small abscesses at the point of infection, and small, yellow nodules in the spleen, liver, lungs, testicles, and mucous membrane of the nose. Implantation of spleen-tissue into other rabbits fixed the period of incubation in this animal at from eleven to twelve days.

Kranzfeld has recently published the results he obtained by inoculations with the virus of glanders in an animal hitherto not subjected to experimentation of this kind. He procured a pure culture from a nodule of a man who had died of glanders after a brief illness. Inoculations were made in a small rodent which is very numerous in the southern part of Russia, the *Spermophilus guttatus*. The course of the disease in this animal was almost the same as in the field-mice that were used by Löffler. Of 28 animals infected with different cultures, 16 died on the fourth day, 9 on the fifth, 2 on the seventh, and 1 on the tenth. The post-mortem appearances were always characteristic: a greenish-gray infiltration at the point of inoculation and a number of nodules in the spleen; in one animal also very small, white nodules in the liver. Cultivations from these nodules yielded a pure growth of the bacillus of glanders. If animals are infected by direct injection of a pure culture into a vein, no serious symptoms are produced; but, if soon thereafter one or more muscles are injured subcutaneously, the microbes escape through the lacerated vessels, localize at the seat of injury, and produce a grave form of the disease. It has been determined by experiment that the farther from the trunk the inoculations are made, the less intense is the local reaction. When an animal is inoculated at a distance from the trunk, and shows no general symptoms, a subcutaneous injury of any portion of the trunk will furnish the necessary conditions for the development of a local form of infection.

It had been generally believed that the intact skin furnished an adequate protection against infection with the bacillus of glanders until shown very recently by the experiments of Babés and Nocard that infection can take place through the healthy skin. Nocard rubbed a pure culture of the bacillus into the skin in two guinea-pigs, and found on the fifteenth day some of the hair-follicles the seat of glanderous inflammation. Histological examination showed numerous bacilli in the follicles, the epithelial layer much thickened, and the surrounding connective tissue in a state of proliferation. The infection had extended from the follicles through the connective tissues into the lymphatic vessels underneath, as was evident from the presence of bacilli in the lymphatic glands, vessels, and connective-tissue spaces in the immediate vicinity of the primary lesion of the skin.

GLANDERS IN THE HORSE.

Glanders and farcy in the horse are different manifestations of the same disease, and, as each of them is divided into an acute and chronic form, we find described four varieties of the disease in this animal,—*acute* and *chronic* glanders, *acute* and *chronic* farcy.

Acute Glanders.—This form of glanders is attended by a high temperature (106° to 109° F.) and other symptoms of acute sepsis, and proves uniformly fatal in a few days. The breathing is accelerated, the pulse feeble and rapid, and there is complete loss of appetite. The nasal mucous membrane, at first of a dark, coppery color, with dark-red ecchymotic patches, becomes purple; these ecchymoses are rapidly converted into ulcers, from which issues a copious sero-sanguinolent discharge. Lymphatic infection is a characteristic feature of acute glanders. The submaxillary and cervical glands enlarge and suppurate, discharging unhealthy-looking, ichorous pus. Abscesses also form in the lymphatics of the face.

Chronic Glanders.—This is the form most commonly seen in the horse. The disease begins in the mucous membrane of the nose. Small, whitish nodules, composed of small, round cells, are formed in the mucous membrane. These nodules soften and ulcerate. Similar nodules may be found in the larynx, trachea, and bronchi. The ulcerations may remain superficial, or they may extend to the deep tissues, even attacking cartilage and bone. The internal organs, especially the lungs, may become the seat of metastatic foci. The left nostril appears to be affected more frequently than the right. The lymphatic glands underneath the lower jaw enlarge very rapidly, often reaching considerable dimensions during a single night. The glandular swellings may continue for several days, afterward slowly disappear, and then re-appear as rapidly as before. The discharge from the nostrils presents a starchy or glue-like appearance, adheres to the mucous membrane, where it dries and accumulates, causing narrowing of the nasal opening.

Acute Farcy.—Acute farcy, together with chronic farcy, is simply another manifestation of glanders, and is initiated in a very similar manner to acute glanders. There are the same lesions of the lymphatics and nodules, and abscesses are found in the skin. A general swelling of the cutaneous tissues takes place, varying in size for a time, but suddenly a number of distinct swellings or nodules will appear, termed "farcy buds." These specific nodules, so characteristic of farcy in either its acute or chronic form, involve the skin, subcutaneous connective tissue, or they may extend to the deeper tissues. They vary in size from a pea to a hazel-nut. These nodules suppurate, and, after evacuation of their contents, leave ragged ulcers that discharge a foul, grayish-white, creamy liquid tinged with blood. When several ulcers are in close proximity they may become confluent and form an extensive ulcerating surface. With the appearance of the nodules the lymphatics become inflamed, swollen, and indurated. Not infrequently acute farcy terminates in the development of acute glanders, with all the pathological conditions that have been described as characteristic of that disease, thus showing their etiological identity.

Chronic Farcy.—In this form of glanders the lymphatic glands are principally involved. The disease is not attended by much febrile disturbance, and all of the other general symptoms are less marked than in the other varieties of glanders. The lymphatic glands become enlarged, and nodules are formed in the skin, lungs, and other viscera. Central softening and suppuration of the nodules is a regular occurrence. Long, fistulous tracts often result from extensive undermining of the skin. In all of these different forms of glanders in the horse the cause remains the same, and the pathological conditions are identical; only the clinical aspects vary from the location, intensity, and extent of the primary infection.

GLANDERS IN MAN.

In man the disease occurs in an acute and chronic form, but does not exactly resembe any of the varieties of the disease in the horse or the disease artificially produced in animals by inoculation. The discharge from the nostrils of a diseased horse, brought in contact with an abraded surface or a mucous membrane, will communicate the disease. Notwithstanding the positive results that followed the cutaneous inoculations in guinea-pigs with a pure culture of the bacilli of glanders by Nocard, it is, for all practical purposes, safe to make the assertion that the virus of glanders can only find entrance into the organism through a wounded surface. Whether infection may not take place through the alimentary canal has, so far, not been definitely ascertained. It is certain that the disease cannot be contracted by eating boiled or fried flesh of animals. Infection through the respiratory organs is possible, as cases have been reported in which the lungs were the primary and only seat of the disease. The fact that man can be infected with a pure culture of the bacilli of glanders as successfully as the animals that have been successfully experimented on received a sad illustration last winter in Vienna.

Dr. Hoffman, a young and promising physician, who was making some experimental investigations on animals with pure cultures, accidentally inoculated himself with the needle used for making the inoculations, and died from acute glanders in a few days. Observations of veterinary surgeons and experimental researches have shown, conclusively, that the disease can be transmitted from the mother to the fœtus *in utero* by passage of the bacilli through the placenta from the maternal into the fœtal circulation. When man is the subject of glanders, bacilli are found more constantly in the blood than in glanderous animals. In the case described by Weichselbaum, numerous bacilli could be seen in the blood. In this case a thrombus was found in one of the large meningeal veins, containing numerous bacilli, and which, undoubtedly, was one of the sources of the bacilli in the circulation. In man the nasal mucous membrane is not so frequently affected as in animals, although Böllinger has shown that in horses the nasal cavity is not always affected, and that it may present a normal condition, even when the larynx and lungs are seriously affected. Muscular abscesses, that may assimilate rheumatism, are a frequent occurrence, especially in the chronic form of the disease.

SYMPTOMS AND DIAGNOSIS.

The symptomatology of glanders is variable, as it is greatly modified by the intensity of the infection, the primary location of the disease, and the number and distribution of the metastatic foci. The disease may begin at a single point, and may then be mistaken for a carbuncle or a gangrenous erysipelas. Græfe reports a case which began as an acute exophthalmos, and the nature of the disease was not ascertained until after death. In this case there were nodules in the choroid of the eye. Acute glanders runs a rapid and malignant course. Infection usually takes place through a small wound-puncture or abrasion about the face or hands. At the point of inoculation a somewhat elongated, soft, inflammatory swelling or nodule forms in a few days. Central softening and suppuration soon transform the inflammatory product into an undermined ulcer, with irregular, ragged margins, surrounded by a wall of infiltration. In mild cases the disease may remain local, and the ulcer heals under proper treatment in a few weeks. In other cases regional infection takes place, and the lymphatic glands become swollen and suppurate, leaving the same kind of ulcers as at the primary seat of infection.

In the fatal cases general infection takes place either through the veins or the lymphatic vessels, and the symptoms then resemble septicæmia or pyæmia, or a combination of these two diseases,—septico-pyæmia. If infection take place directly through the veins, a thrombo-phlebitis develops in connection with one of the nodules and the bacilli in the thrombus, which multiply in this nutrient medium and gain entrance into the general circulation singly or through the medium of infected emboli. Under such circumstances, nodules are found in the lungs, kidneys, and other internal organs, as suppurating metastatic deposits in muscles, bone, joints, and testicle. In such cases the general symptoms may simulate to perfection typhoid fever, pyæmia, suppurative osteomyelitis, and acute general miliary tuberculosis. In acute cases, where general infection occurs early and rapidly, death results in from one to three or four weeks, while in chronic cases the final fatal termination is often postponed for months. In illustration of the clinical history of this disease I will quote briefly a few cases.

A Russian medical journal of recent date states that a young soldier, who had been a wagoner before his admission into the army, was received into the military hospital suffering from two foul ulcers on the hard palate, which had perforated the nasal fossa and destroyed the inferior turbinated bones. Three weeks later a swelling appeared over the eyebrow; a fortnight afterward he complained of pain on the inner side of the left knee, around the internal tuberosity of the tibia. A purulent discharge occurred from the left ear, and, at the same time, an abscess developed on the back of the right hand which appeared as a deep-purple tubercle, with a hard circumference, and sunken toward the centre; a purulent discharge oozed from the surface. At first, for a short time after admission, the temperature varied, rising in the evening to 103° to 104° F.; later on it fell to normal. The disease was mistaken for syphilis, and iodide of potassium was given without the least benefit. About ten weeks after admission he was in better health, and left the hospital, receiving his discharge from the army. Within a few weeks he returned, with extension of ulceration of the hard palate; the uvula was destroyed. The characteristic nodules, the "farcy buds," appeared in the face; the metastatic abscess on the back of the hand remained. The patient ultimately died of exhaustion. Before death some of the nodules were extirpated; they were found to contain micro-organisms resembling to perfection the bacillus of Löffler and Schütz.

Küttner reports a number of cases in which the skin was the seat of numerous points of suppuration in the form of pustules, or more diffuse abscesses followed by ulceration. The disease has been mistaken more frequently for syphilis than any other affection. This mistake in diagnosis is very liable to be made in the chronic form, in which the nodules grow very slowly, are hard, and may occur in groups or like a string of beads. The nodules usually soften, and form chronic ulcers, that closely resemble the ulcers resulting from the breaking down of gummata. If the disease primarily attack the nasal cavity, the mucous membrane presents hard nodules, and a copious discharge from the nose is present. In acute glanders affecting the nose and face, extensive destruction of tissue by the rapid breaking down of the nodules is one of the prominent clinical features of the disease. Complete destruction of the nose, with formation of large ulcers of the face, may happen in the course of a week.

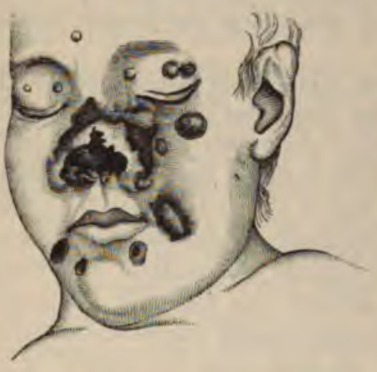

FIG. 109.—ACUTE GLANDERS, INVOLVING NOSE AND FACE, SHOWING EXTENT OF LOCAL LESIONS EIGHT DAYS AFTER THE COMMENCEMENT OF THE FIRST SYMPTOMS. (*Birch-Hirschfeld.*)

Chronic glanders may also be easily mistaken for tuberculosis of the skin, mucous membranes, and lymphatic glands. Acute glanders may simulate furuncle, carbuncle, and other acute suppurative lesions, as well as lymphangitis and erysipelas. In making a differential diagnosis between these different affections and glanders, it is important, if possible, to trace the infection to its proper source. If the clinical history point to the possibility of infection by contact with a glanderous horse, it should be remembered that the period of incubation in man varies from two days to three weeks. A positive diagnosis must necessarily rest on the detection of the specific microbe in the granulation tissue or in the discharges, and the results obtained by inoculation experiments. As soon as general infection has taken place, the symptoms resemble pyæmia or septicæmia; so that a differential diagnosis between metastatic glanders and general infection with pus-microbes cannot be made without the aid of the microscope and inoculation experiments.

PATHOLOGY AND MORBID ANATOMY.

The bacillus of glanders resembles, in its immediate action on the tissues, both the bacillus of tuberculosis and the pus-microbes. The histological change first observed in the infected tissues is a transformation of mature into embryonal tissue, the microscopical picture, with the exception of the absence of giant cells, resembling tubercle; but this stage is of short duration, as the pyogenic effect of the bacillus of glanders soon produces purulent softening by the speedy conversion of the embryonal cells and leucocytes into pus-corpuscles. The formation of abscesses is a constant occurrence, wherever localization has taken place, either by direct infection, secondary infection from regional diffusion through the lymphatic vessels and connective-tissue spaces, or by general infection by embolic diffusion through the general circulation.

As soon as the disease has become general, the clinical picture and pathological conditions are the same as in pyæmia caused by a suppurative lesion. The differentiation between the two forms of metastasis can be made only by demonstrating the primary cause, by use of the microscope, or by the results obtained from inoculation experiments. The pus found in glanders is grayish red in color, and quite tenacious in recent lesions, but after opening the abscesses it assumes the character of ordinary pus, as the abscess-cavities then become the seat of secondary infection with pus-microbes. Swelling and abscesses of the testicles have been frequently observed in cases where the disease has become general, the affection in these organs being one of the clinical manifestations that embolic dissemination has occurred. Primary glanders of the lungs from inhalation of the microbes into the air-passages gives rise to symptoms and pathological conditions that cannot be distinguished from pulmonary tuberculosis, unless the essential cause can be demonstrated in the sputa under the microscope, or glanders can be artificially produced by the injection of sputum into the subcutaneous tissue or the peritoneal cavity of guinea-pigs. The pulmonary nodules soften and suppurate, and cavities form in the same manner as in pulmonary tuberculosis.

PROGNOSIS.

The prognosis in glanders should always be guarded, as a limited local lesion may be followed by a fatal form of general infection. The prognosis is comparatively favorable if the infection remain limited to a circumscribed area accessible to direct surgical treatment. It must be more guarded if regional infection through the lymphatic vessels has occurred, and it is absolutely fatal in cases of primary glanders of important internal organs, and when general infection has followed in the course of a local lesion with or without regional dissemination. In the local form of the disease the ulcerations usually prove inveterate to treatment, and final recovery is often retarded for months by extensive undermining of the skin. Acute glanders with general infection, as a rule, proves fatal within one to three weeks, and death occurs in consequence of septic infection.

TREATMENT.

The prophylactic treatment consists in preventing infection from glanderous horses and substances which have become contaminated with the specific virus from diseased animals, and requires early recognition of the disease and killing of the affected animals, as well as thorough disinfection of the premises occupied by the diseased beast. The cadavers should be cremated or deeply buried. Abrasions or granulating surfaces that have been exposed to infection should be cauterized.

In cases of primary pulmonary or intestinal glanders, and after general infection from a local form of the disease has occurred, the treatment must be necessarily symptomatic, as such cases are beyond the reach of local or general treatment. The embarrassed respiration and feeble and rapid pulse indicate the use of alcoholic stimulants. A primary nodule should be removed by excision, taking all necessary precautions to prevent infection of the wound in case the skin has been destroyed by ulceration. Limited regional infection should be treated in the same manner if ulceration has not taken place, and the conditions are such that all of the infected tissues can be removed with safety.

After multiple abscesses have formed a radical operation is no longer indicated, the extent of the affection precluding the possibility of removing all of the infected tissues. In such cases the abscesses should be freely incised, fistulous tracts laid open, undermined skin cut away, and, as far as possible, the infected tissues removed with a sharp spoon; then the entire surface should be disinfected with a 12-per-cent. solution of chloride of zinc. No attempt should be made, under such circumstances, to obtain healing of the superficial wounds until it becomes apparent that the specific microbic cause has been eliminated or destroyed, and several repetitions of the curetting and disinfection may become necessary until this object is realized. The scraped surfaces should be kept covered with a moist antiseptic compress gauze, wrung out of 1-to-2000 solution of corrosive sublimate or a 2-per-cent. solution of carbolic acid. If the prolonged use of these antiseptics is objectionable, on account of danger from absorption of toxic doses of drugs, strong iodine-water can be used in the same way. The internal use of iodine, creasote, and arsenic have been recommended as specifics in the treatment of glanders, but clinical experience has not supported this claim, and the surgeon must rely upon local measures in his efforts to protect the patient against the dangers arising from regional and general infection; while he must aim, at the same time, to maintain the resisting power of the tissues to the microbic invasion by a supporting tonic and stimulating treatment.

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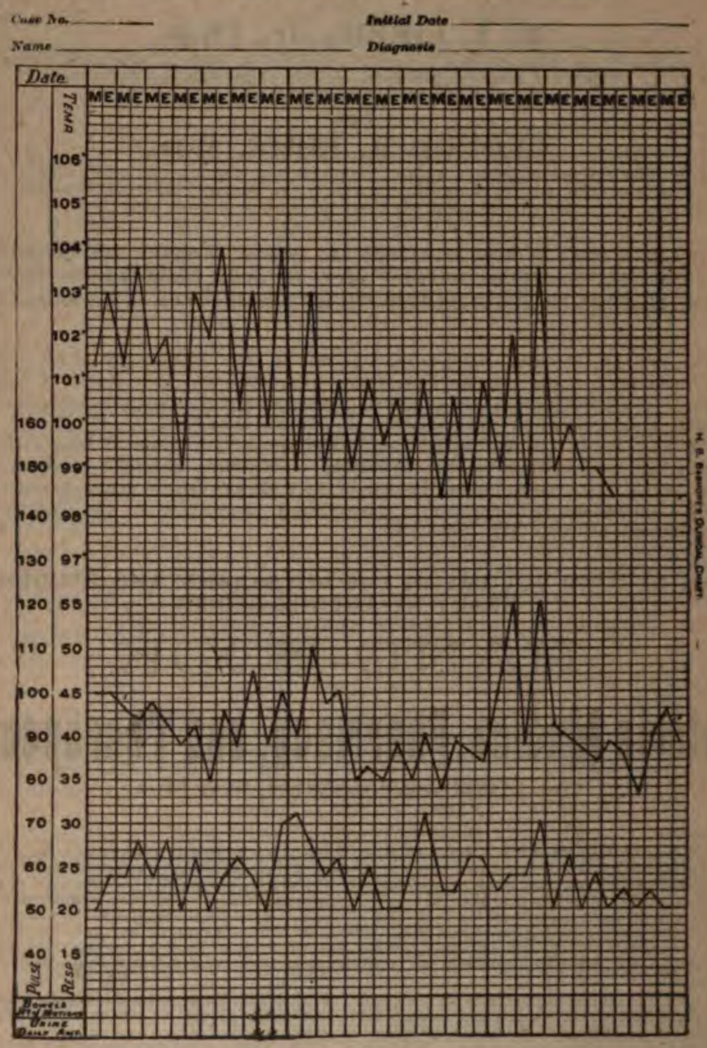

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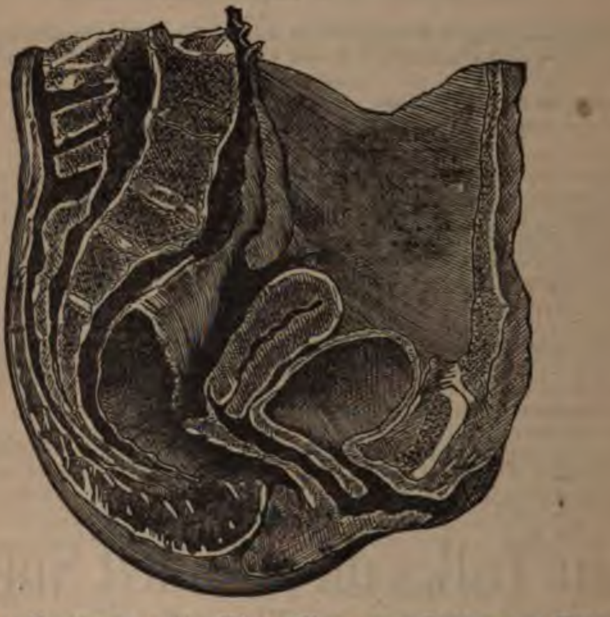

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(a) Aconitine.	Narcotic and Apyretic.	1-500 gr.	1–16 gr.

Following this, Preparations of the Pharmacopœia, each tabulated. For example:

TINCTURAL.

TINCTURA.	DRUG.	AMOUNT.	ALCOHOL.	DOSE.
* Aconiti.	Aconite. Tartaric Acid, 60 † P.	5½ oz. to 24 gr.	100	1 to 3 drops.

* 60 Fineness of Powder as per U. S. P.

† P. Macerate 24 hours. Percolate, adding Menstruum to complete (1) pint tincture.

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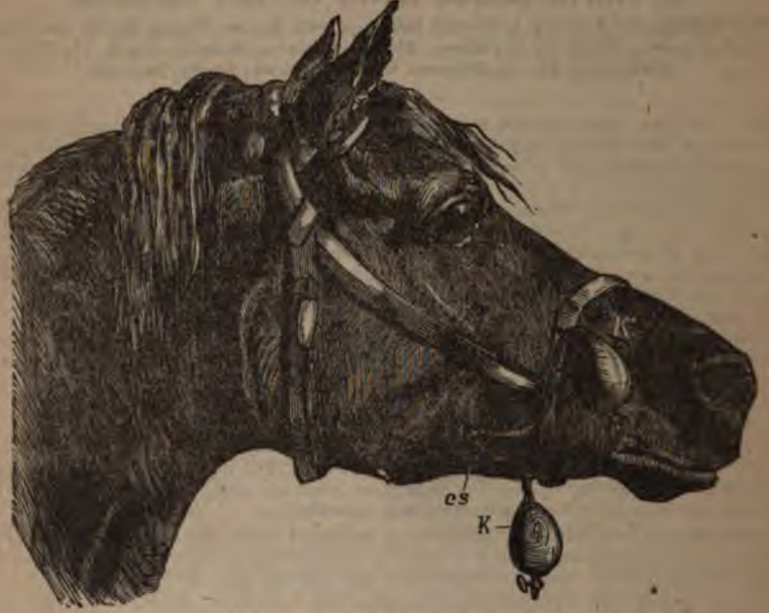

FIG. 117.—PAROTID AND SUBMAXILLARY FISTULÆ IN THE HORSE, AFTER COLIN. (*Thanhoffer and Tormay.*)
K, K', rubber bulbs for collecting saliva; *cs*, cannula in the parotid duct.

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